

08/484337

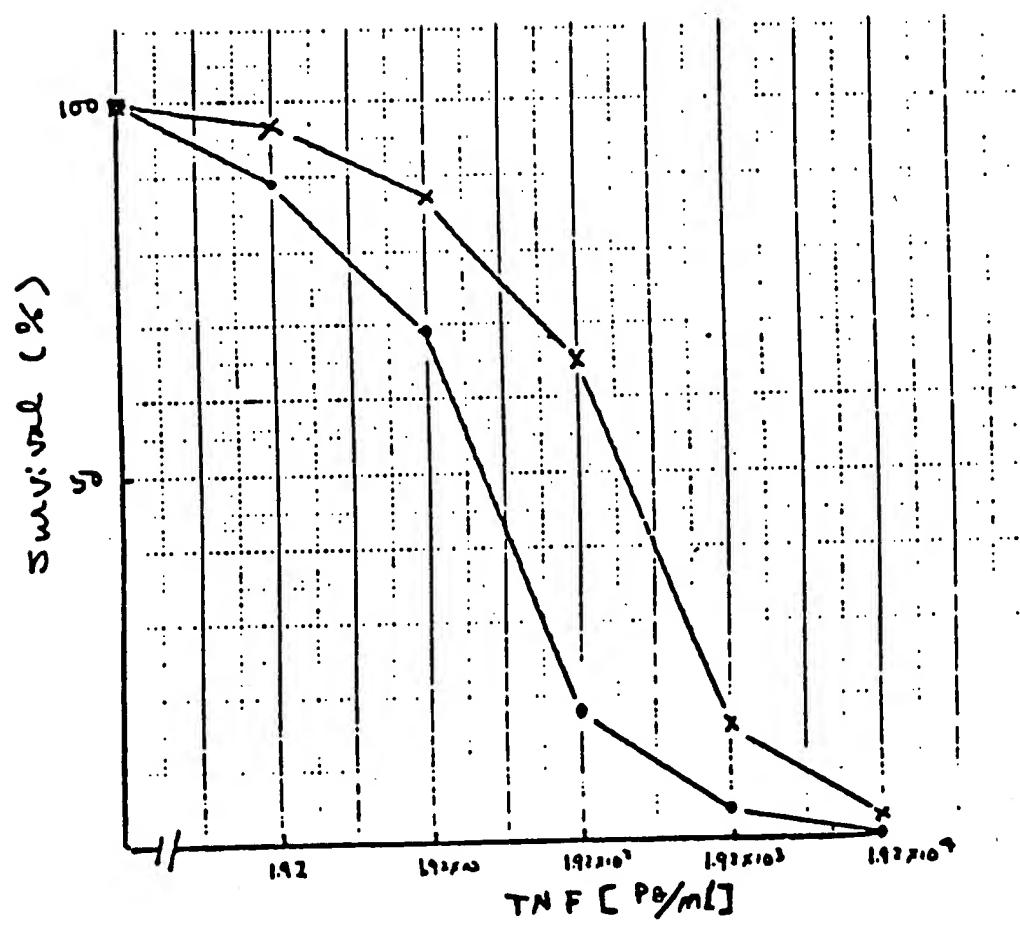


FIG. 1

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b. a. ⊖



⊕

FIG. 2

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a b c d.



FIG. 3

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a b c d.

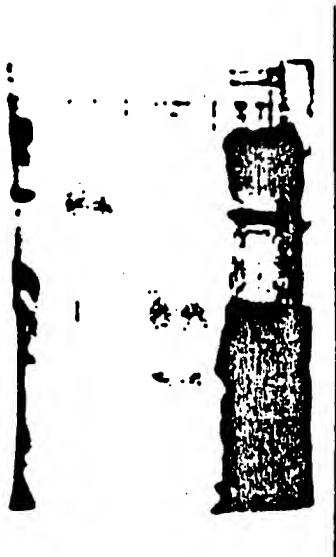


FIG 4

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a. b.

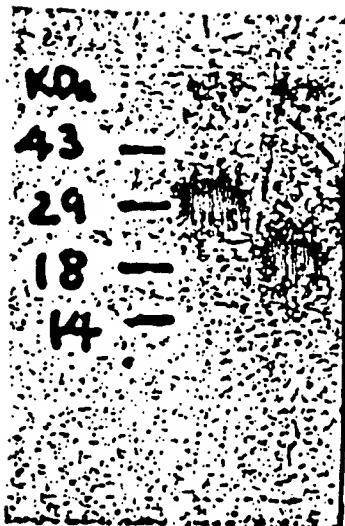
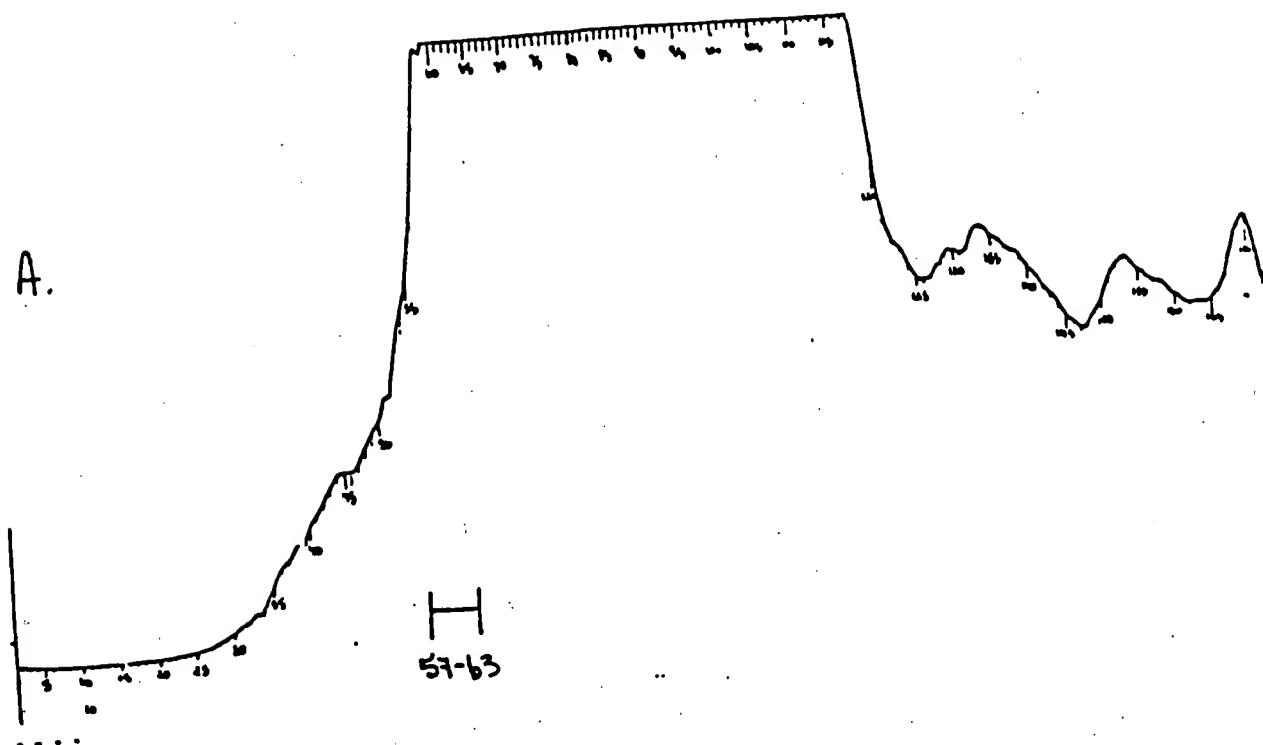


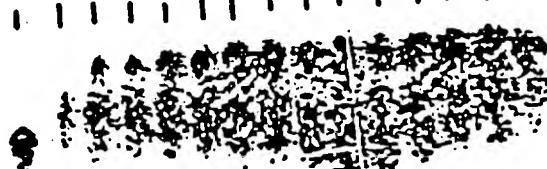
FIG. 5

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Figure 6



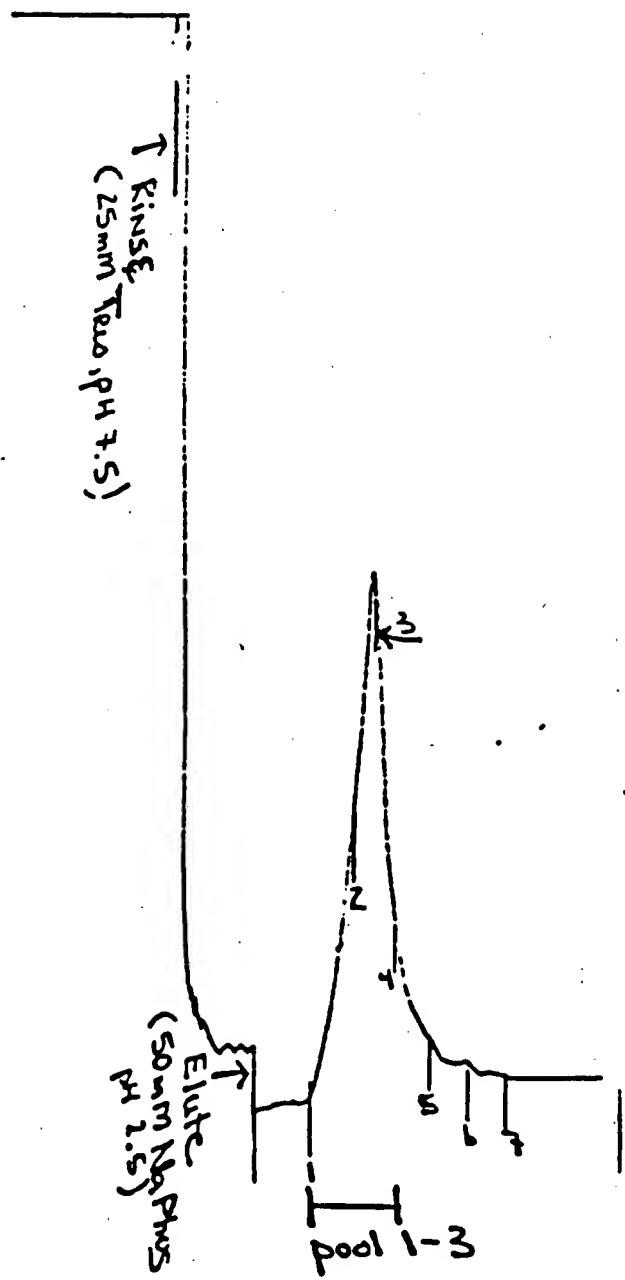
+ 1 45 47 49 51 53 55 57 59 51 53 55 57 59



B.

08/484337

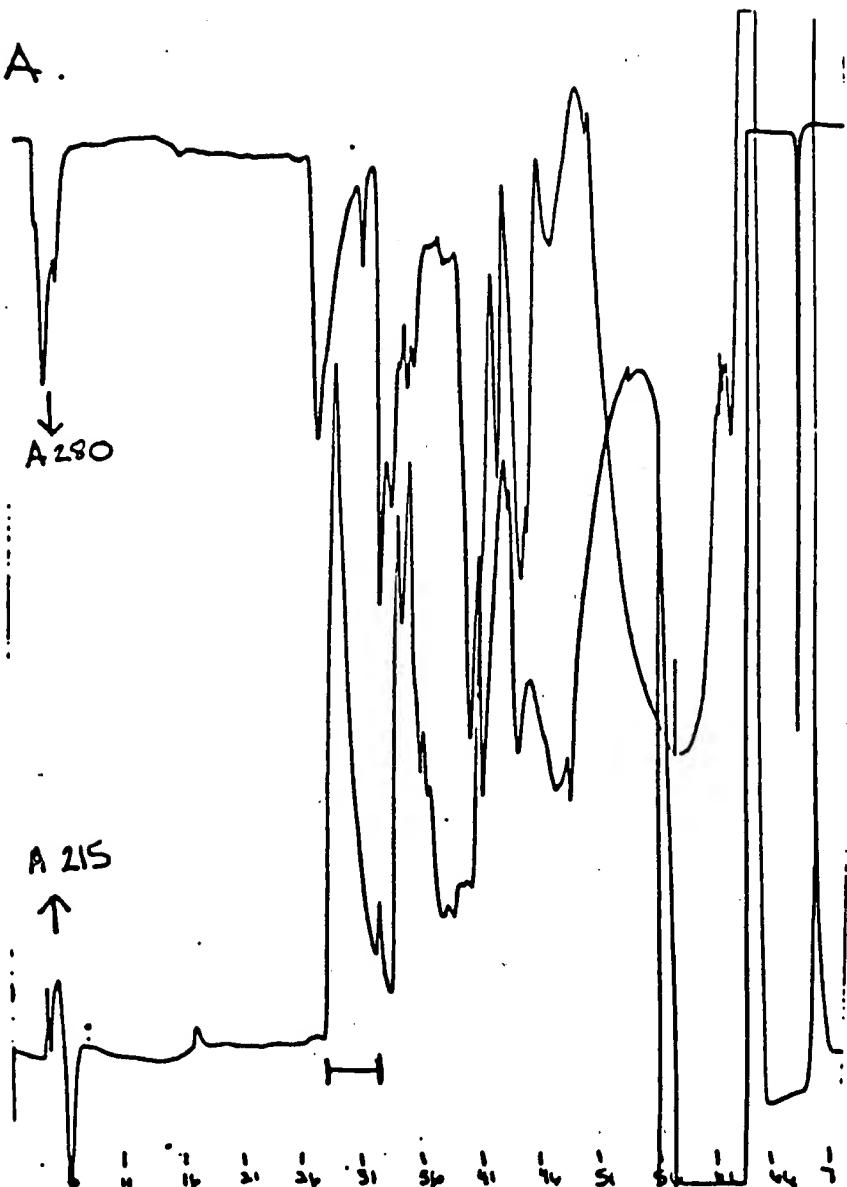
Figure 7



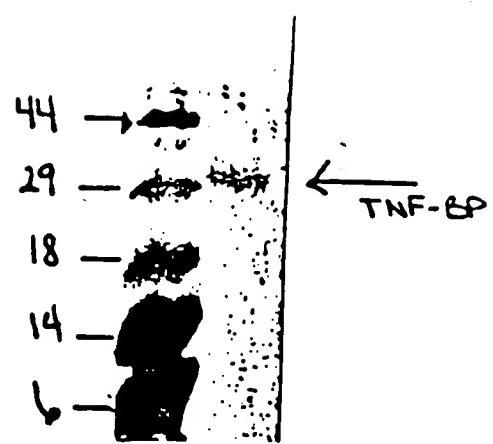
08/484337

Figure 8

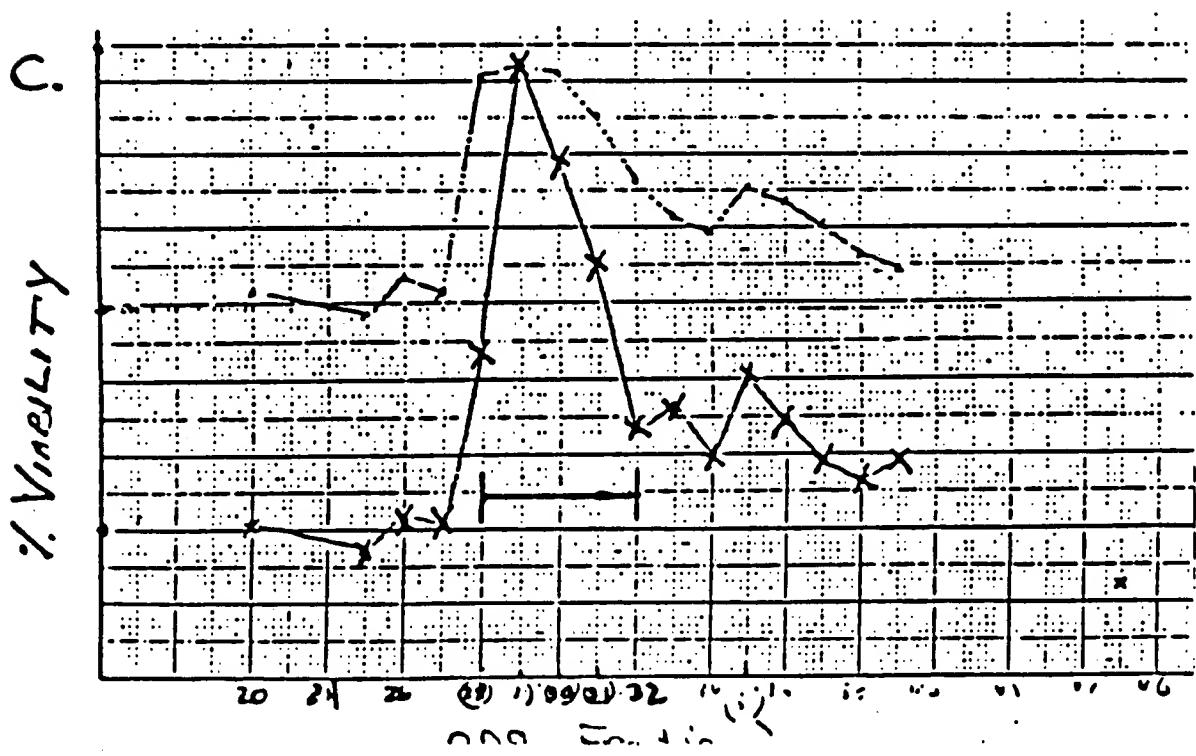
A.



B.



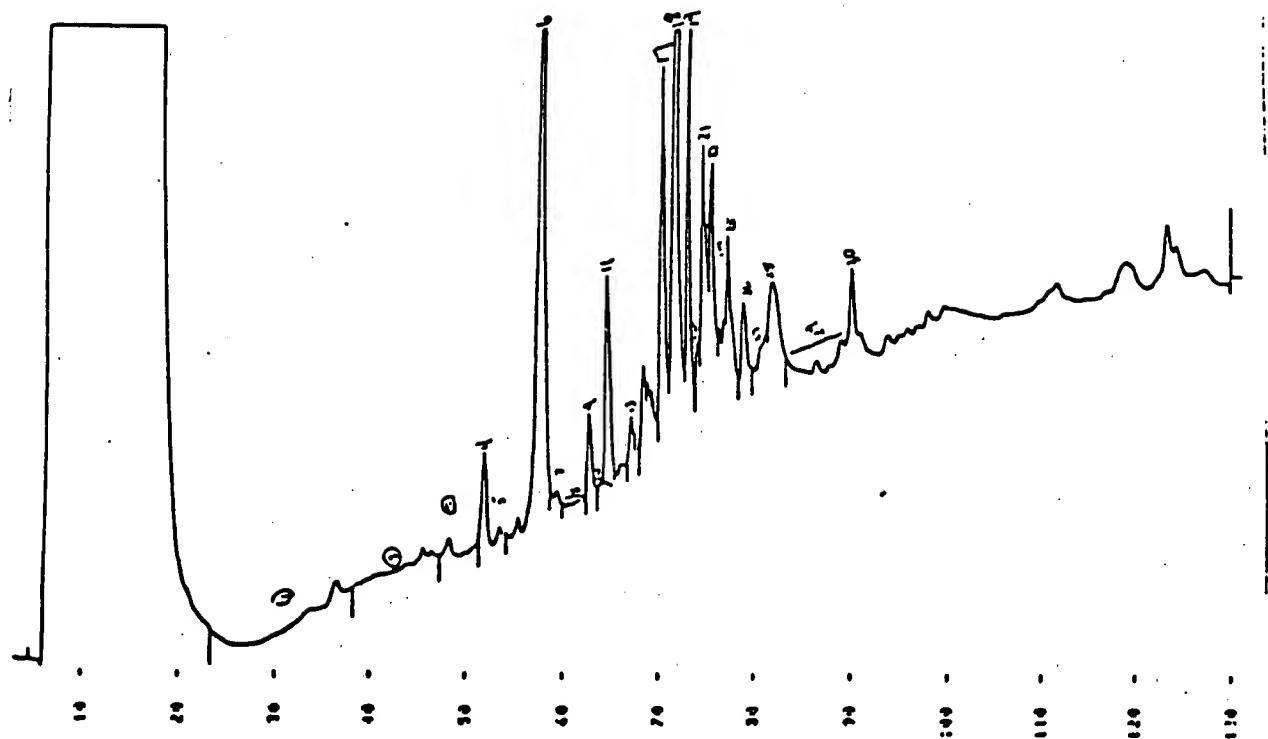
C.



8/484337

st

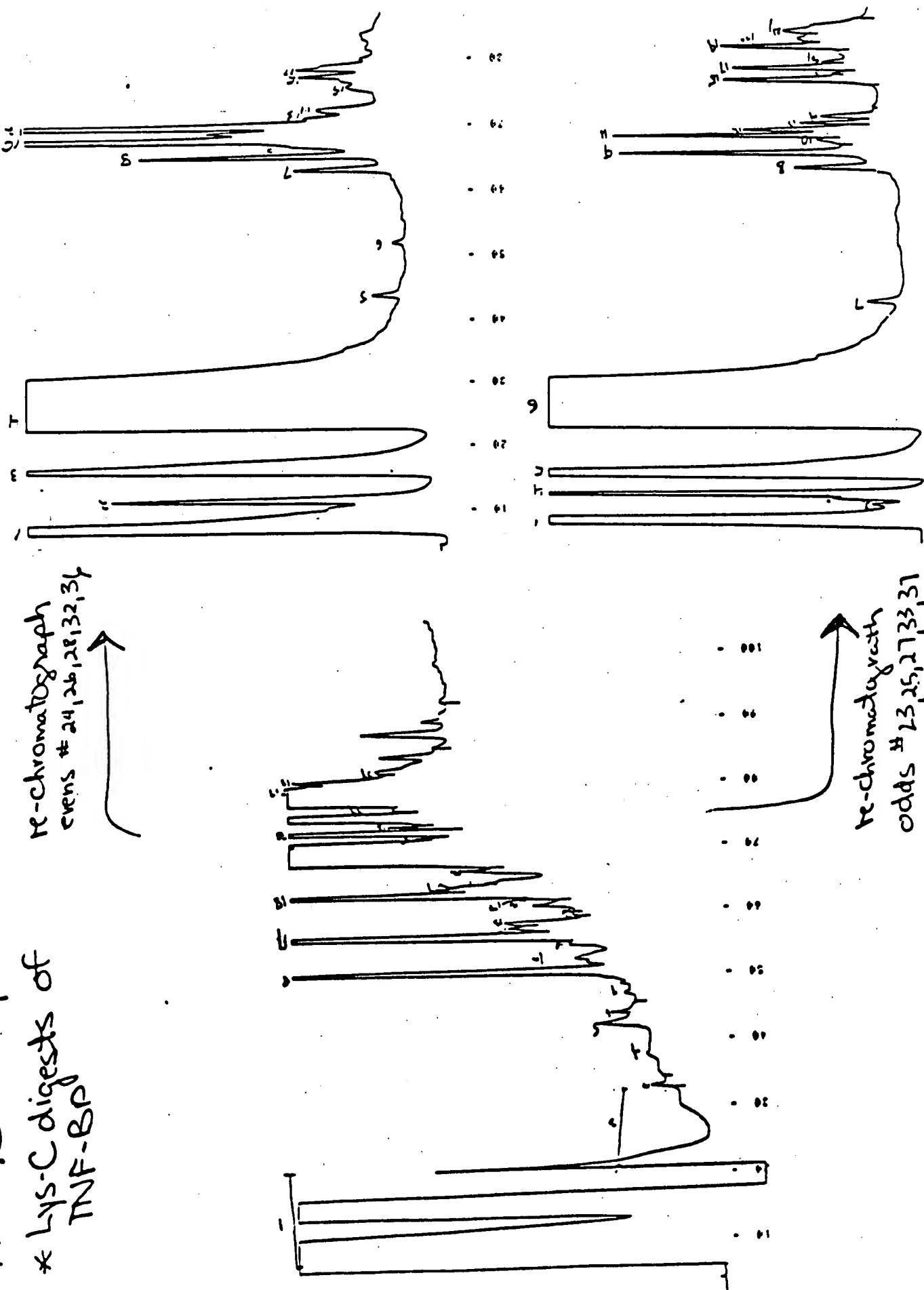
FIG. 9A



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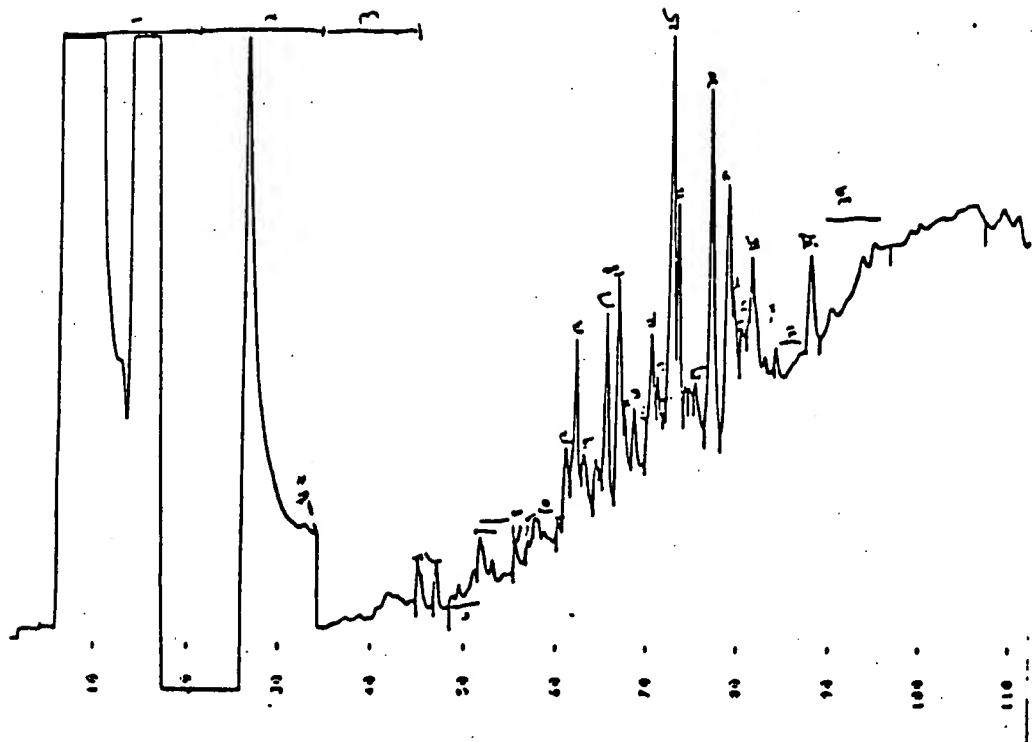
Fig 9B : ALKYLATED

* Lys-C digests of
TNF-Bo

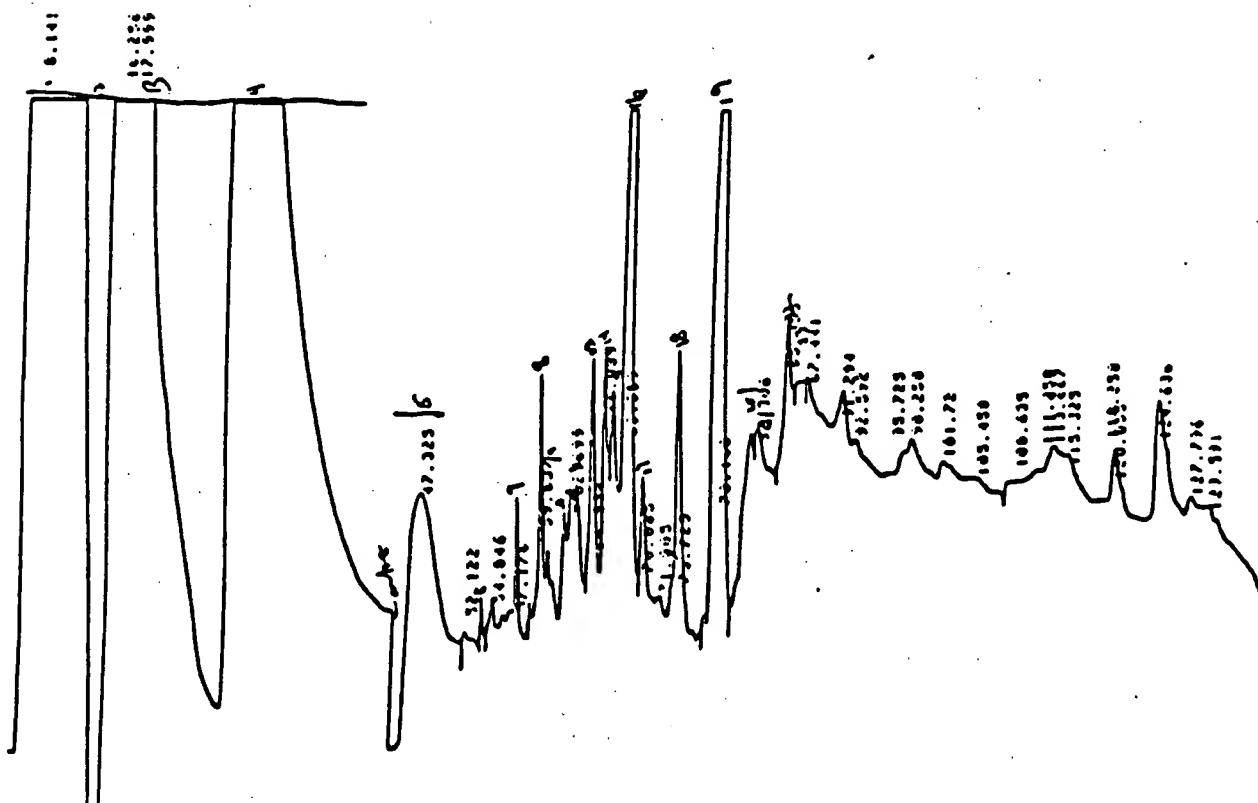


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FIG. 10



1



#2

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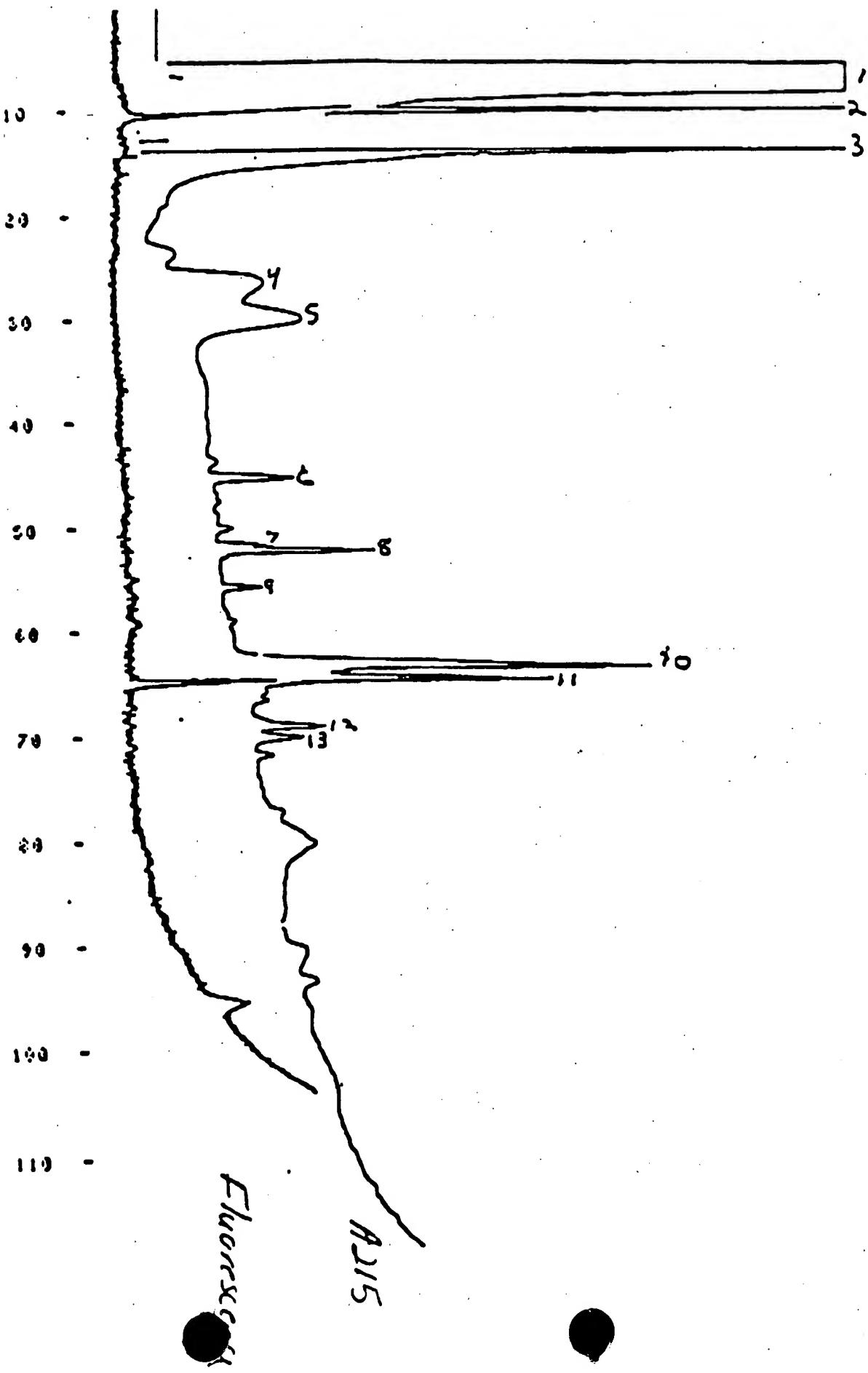


FIG. // A

Fig. 11B

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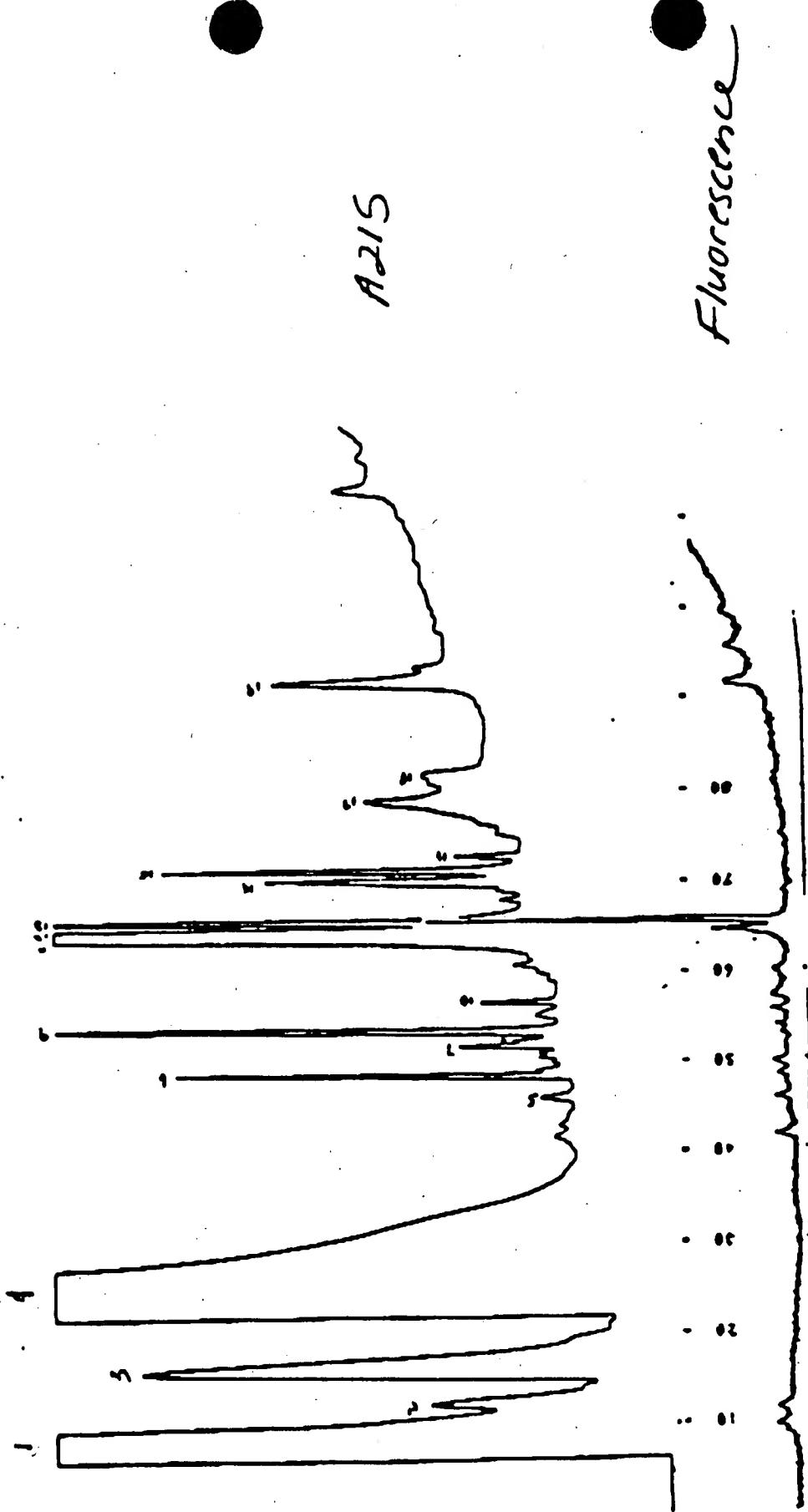


Figure 12

- A. 1 10 20 30 40 50 60
B. S S V C P A C K T I S P A N N I C C T K C K G T Y H D C P P E D I E C - - - S C S F T A S E E R L R I C C S - - - K -
C. (T) E N C O V E R C F L A N E E C V S C (L) N C (K) (E) (C) (L) (K) (E) (S)
(G)
(K) (S) L E C T R I C L P O I E U - (S) (H) P (S) (A)
(D) (A) (G)

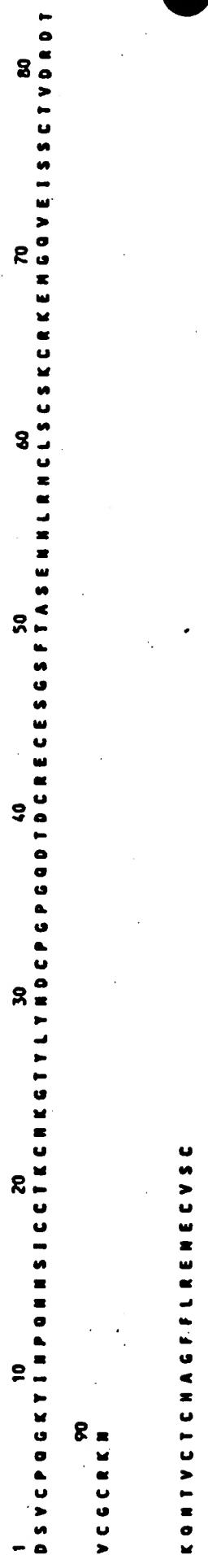
08/484337

10	20	30	40	50	60	70
CA1GCCCTGAA GGTCGACTCT AGAGGATCTG GGUCCTACTA GCTTTGAGTT GAGGGAAACAA AAATTAACAC						
80	90	100	110	120	130	140
ACAGGAAAC TAGAGAACAA TTAAGCATCA GATTATATGC CCCAACTGTC TAAGTTCAA GGAAGAACTC						
150	160	170	180	190	200	210
TAAACTTAGT GAATGGCGTG GCCTGGGCCG AATGTTTCAAC TGAGGAAGGA CTTGAUCCAG GGAAGTTTA						
220	230	240	250	260	270	280
GATCTGCTAC CCCTAACGTT CCCATCCCCTC CCTCTCTTGA TGGTGTCTCC TCTATCTGAT TCTTCCCCAG						
290	298	307	316	325	334	
GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG ATT ATT GGA CTC GTC Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val						
343	352	361	370	379	388	
CTT CAC CTA GGG GAC AGG GAG AAG AGA GAT AGT GTG TGT CCC CAA GCA AAA TAT Pro His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys Tyr						
397	406	415	424	433	444	
ATC CAC CCT CAA AAT ATT TCG ATT TGC TGT ACU AAA UGC CAC AAA G GTAGGGGCAA Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys Cys His Lys Ala						
454	464	474	484	494	504	514
GTUGAAACGG TGAATGCCCT CAGGTCTGGG GTGCTGCTTC TTTCTCTGCT TCTTCCAGTT GTCTTCCCT						
524	534	544	554	564	574	584
AACTTTGCTG TCTCTCTGG GUTGGGATTY TCTCCCTCCC TCCCTCTCTA GAGACTTCAG GGAATCGGCC						
594	604	614	624	634	644	654
CTGGC1GTTG TCCCTAGCAT GGGGCTCTT CCTTGTGTT TCACCCGCAG CCTAACTCTG CGGCCCCATT						
664	673	682	691	700		
CA CA GAA ACC TAC TTG TAC ATT GAC TGT CCA GGC CGG GGG CAG GAT ACG GAC Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gln Asp Thr Asp						
709	718	727	736	745	754	
TGC AGG GAG TGT GAG AGC GGC TCA TTC ACC GCT TCA GAA AAC CAC CTC AGA CAC Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His						
763	772	781	790	807	817	
TGC CTC AGC TGC TCC AAA TGC CCA AAG GGTGAGTGTG CACAGGCAGG AGAGTCAGGC Cys Leu Ser Cys Ser Lys Cys Arg Lys						
827	837	847	857	867	877	887
GAGCTTCAAG TGGTGTGTGG GTGCTGCTCT ATGTGCAGGC TGGTGGGTGT GGGCAGUAAG GTGTGTGT						
897	907	917	927	937	947	957
TGTGUGACCA CTGCTATGGAT GTGAGTGTGT ATTACAGAGA CACACACTTA GGGGTATGTC AGAAAAGGAA						
967	977	987	997	1007	1017	
TGCAGUGACCA GGGUGAAGCA GAACTCATAC CCCATCTCTC CCCCTCACCA GAA ATA GAT CAG Glu MET Glu Gln						
1029						
GTC GAA AIC V+I Glu Ile						

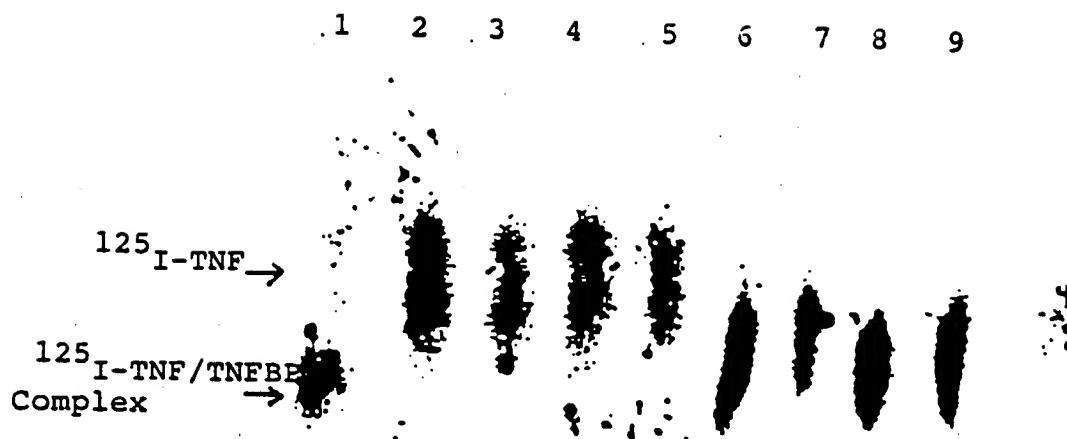
FIG. 13

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FIG. 14



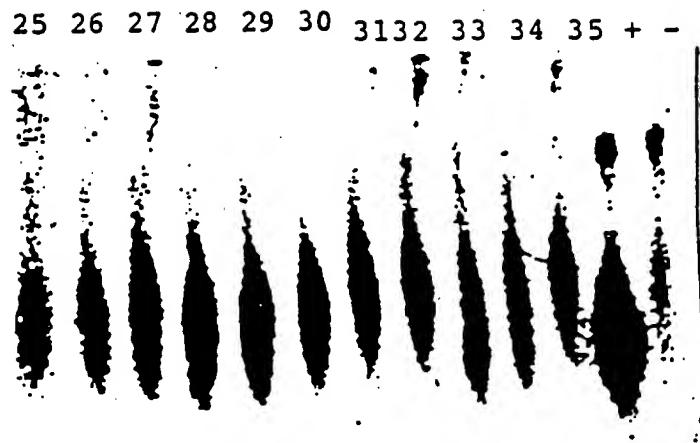
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Lane 1 is a positive control. Purified TNF-BP complexed with ^{125}I -TNF. Lane 2-5 are protein from the 24, 48, 72, and 96 hour incubations with PMA/PHA that did not bind to the TNF-affinity column. Lane 6-9 are the material from the same incubations that did bind to the TNF-affinity column.

Figure 15

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Fractions 27, 28 and 29, 33 and 34 show TNF binding activity. + is as lane 1 of figure 15. - is ^{125}I -TNF alone.

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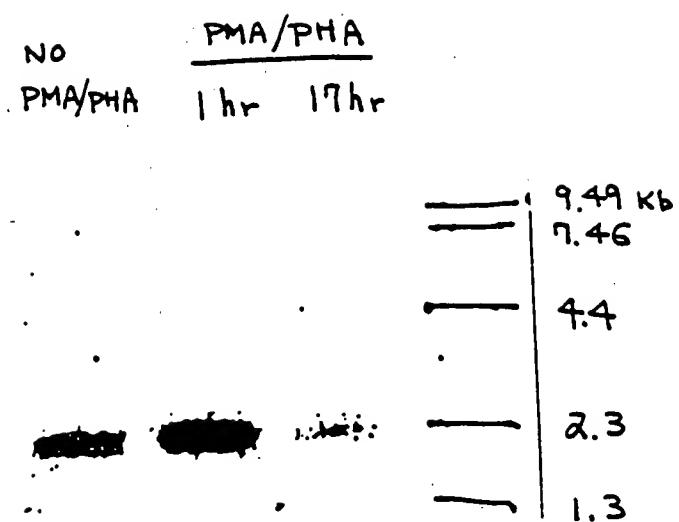


Fig 17

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11 21 51 12 22 52



FIG 18

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Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr
10 20
Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp
30 40
Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu
50 60
Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp
70 80
Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu
90 100
Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu
110 120
Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val
130 140
Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu
150 160
Asn

FIG 19

				296	305
				GAT AGT GTG TGT CCC CAA	
				Asp Ser Val Cys Pro Gln	
314	323	332	341	350	359
GGA AAA TAT ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC AAG TGC CAC AAA					
Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys					
368	377	386	395	404	413
GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACG GAC TGC AGG					
Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp Cys Arg					
422	431	440	449	458	467
GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AGA CAC TGC CTC					
Glut Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu					
476	485	494	503	512	521
AGC TGC TCC AAA TGC CGA AAG GAA ATG GGT CAG GTG GAG ATC TCT TCT TGC ACA					
Ser Cys Ser Lys Cys Arg Lys Glu MET Gly Gln Val Glu Ile Ser Ser Cys Thr					
530	539	548	557	566	575
GTC GAC CGG GAC ACC GTG TGT GGC TGC AGG AAG AAC CAG TAC CGG CAT TAT TGG					
Val Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp					
584	593	602	611	620	629
AGT GAA AAC CTT TTC CAG TGC TTC AAT TGC AGC CTC TGC CTC AAT GGG ACC GTG					
Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Glu Thr Val					
638	647	656	665	674	683
CAC CTC TCC TGC CAG GAG AAA CAG AAC ACC GTG TGC ACC TGC CAT GCA GGT TTC					
His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr Cys His Ala Glu Phe					
692	701	710	719	728	737
TTT CTA AGA GAA AAC GAG TGT GTC TCC TGT AGT AAC TGT AAG AAA AGC CTG GAG					
Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Ser Leu Glu					
746	755	764			
TGC ACG AAG TTG TGC CTA CCC CAG ATT GAG AAT					
Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu Asn					

Figure 20.

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10 20 30 40 50 60 70

GATCACTGGG ACCAGGGGT GATCTCTATG CCCGAGTCAC ACCCTCAAC TGTCAACCCAA AGGCACCTGG

80 90 100 110 120 130 140

GACGTCTGG ACAGACCGAG TCCCCGGGAAG CCCCAGCACT GCCGCTGCCA CACTGCCCTG AGCCCCAAATG

150 160 171 180 189 198

GGGGAGTGAG AGGCCATAGC TGTCTGGC ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG
MET Gly Leu Ser Thr Val Pro Asp Leu Leu

207 216 225 234 243 252

CTG CCG CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT
Leu Pro Leu Val Leu Leu Glu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile

261 270 279 288 297 306

GGA CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA GAT AGT GTG TGT CCC CAA
Gly Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln

315 324 333 342 351 360

GGA AAA TAT ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC AAG TGC CAC AAA
Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys

369 378 387 396 405 414

GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACG GAC TGC AGG
Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gln Asp Thr Asp Cys Arg

423 432 441 450 459 468

GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AGA CAC TGC CTC
Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu

477 486 495 504 513 522

AGC TGC TCC AAA TGC CGA AAG GAA ATG GGT CAG GTG GAG ATC TCT TCT TGC ACA
Ser Cys Ser Lys Cys Arg Lys Glu MET Gly Gln Val Glu Ile Ser Ser Cys Thr

531 540 549 558 567 576

GTC GAC CGG GAC ACC GTG TGT GGC TGC AGG AAG AAC CAG TAC CGG CAT TAT TGG
Val Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp

585 594 603 612 621 630

AGT GAA AAC CTT TTC CAG TGC TTC AAT TGC AGC CTC TGC CTC AAT GGG ACC GTG
Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val

639 648 657 666 675 684

CAC CTC TCC TGC CAG GAG AAA CAG AAC ACC GTG TGC ACC TGC CAT GCA GGT TTC
His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe

Fig 21

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693	702	711	720	729	738
TTT CTA AGA GAA AAC GAG TGT GTC TCC TGT AGT AAC TGT AAG AAA AGC CTG GAG					
Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu					
747	756	765	774	783	792
TGC ACG AAG TTG TGC CTA CCC CAG ATT GAG AAT GTT AAG GGC ACT GAG GAC TCA					
Cys Thr Lys Leu Cys Leu Pro Gin Ile Glu Asn Val Lys Gly Thr Glu Asp Ser					
801	810	819	828	837	846
GGC ACC ACA GTG CTG TTG CCC CTG GTC ATT TTC TTT GGT CTT TGC CTT TTA TCC					
Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu Leu Ser					
855	864	873	882	891	900
CTC CTC TTC ATT GGT TTA ATG TAT CGC TAC CAA CGG TGG AAG TCC AAG CTC TAC					
Leu Leu Phe Ile Gly Leu MET Tyr Arg Tyr Gln Arg Trp Lys Ser Lys Leu Tyr					
909	918	927	936	945	954
TCC ATT GTT TGT GGG AAA TCG ACA CCT GAA AAA GAG GGG GAG CTT GAA GGA ACT					
Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu Gly Glu Leu Glu Gly Thr					
963	972	981	990	999	1008
ACT ACT AAG CCC CTG GCC CCA AAC CCA AGC TTC AGT CCC ACT CCA GGC TTC ACC					
Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser Phe Ser Pro Thr Pro Gly Phe Thr					
1017	1026	1035	1044	1053	1062
CCC ACC CTG GGC TTC AGT CCC GTG CCC AGT TCC ACC TTC ACC TCC AGC TCC ACC					
Pro Thr Leu Gly Phe Ser Pro Val Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr					
1071	1080	1089	1098	1107	1116
TAT ACC CCC GGT GAC TGT CCC AAC TTT GCG GCT CCC CGC AGA GAG GTG GCA CCA					
Tyr Thr Pro Gly Asp Cys Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro					
1125	1134	1143	1152	1161	1170
CCC TAT CAG GGG GCT GAC CCC ATC CTT GCG ACA GCC CTC GCC TCC GAC CCC ATC					
Pro Tyr Gln Gly Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile					
1179	1188	1197	1206	1215	1224
CCC AAC CCC CTT CAG AAG TGG GAG GAC AGC GCC CAC AAG CCA CAG AGC CTA GAC					
Pro Asn Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp					
1233	1242	1251	1260	1269	1278
ACT GAT GAC CCC GCG ACG CTG TAC GCC GTG GTG GAG AAC GTG CCC CCG TTG CGC					
Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro Leu Arg					
1287	1296	1305	1314	1323	1332
TGG AAG GAA TTC GTG CGG CGC CTA GGG CTG AGC GAC CAC GAG ATC GAT CGG CTG					
Trp Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu Ile Asp Arg Leu					

1341	1350	1359	1368	1377	1386												
<hr/>																	
GAG	CTG	CAG	AAC	GGG	CGC	TGC	CTG	CGC	GAG	GCG	CAA	TAC	AGC	ATG	CTG	GCG	ACC
Glu	Leu	Gln	Asn	Gly	Arg	Cys	Leu	Arg	Glu	Ala	Gln	Tyr	Ser	MET	Leu	Ala	Thr
<hr/>																	
1395	1404	1413	1422	1431	1440												
<hr/>																	
TGG	AGG	CGG	CGC	ACG	CCG	CGG	CGC	GAG	GCC	ACG	CTG	GAG	CTG	CTG	GGA	CGC	GTG
Trp	Arg	Arg	Arg	Thr	Pro	Arg	Arg	Glu	Ala	Thr	Leu	Glu	Leu	Leu	Gly	Arg	Val
<hr/>																	
1449	1458	1467	1476	1485	1494												
<hr/>																	
CTC	CGC	GAC	ATG	GAC	CTG	CTG	GGC	TGC	CTG	GAG	GAC	ATC	GAG	GAG	GCG	CTT	TGC
Leu	Arg	Asp	MET	Asp	Leu	Leu	Gly	Cys	Leu	Glu	Asp	Ile	Glu	Glu	Ala	Leu	Cys
<hr/>																	
1503	1512	1521	1530		1546	1556											
<hr/>																	
GGC	CCC	GCC	GCC	CTC	CCG	CCC	GCG	CCC	AGT	CTT	CTC	AGA	TGA	GGCTGCGCCCC	CTGCGGGCAG		
Gly	Pro	Ala	Ala	Leu	Pro	Pro	Ala	Pro	Ser	Leu	Leu	Arg	.				
<hr/>																	
1566	1576	1586	1596	1606	1616	1626											
<hr/>																	
CTCTAAAGGAC	CGTCCTGCGA	GATGCCCTTC	CAACCCCCACT	TTTTTCTGGA	AAGGAGGGGT	CCTGCAGGGG											
<hr/>																	
1636	1646	1656	1666	1676	1686	1696											
<hr/>																	
CAAGCAGGAG	CTAGCAGCCG	CCTACTTG GT	GCTAACCCCT	CGATGTACAT	AGCTTTCTC	AGCTGCCTGC											
<hr/>																	
1706	1716	1726	1736	1746	1756	1766											
<hr/>																	
GCGCCGCCGA	CAGTCAGCGC	TGTGCGCGCG	GAGAGAGGTG	CGCCGTGGGC	TCAAGAGCCT	GAGTGGGTGG											
<hr/>																	
1776	1786	1796	1806	1816	1826	1836											
<hr/>																	
TTTGCAGGGA	TGAGGGACGC	TATGCCTCAT	GCCCCGTTTG	GGTGTCCCTCA	CCAGCAAGGC	TGCTCGGGGG											
<hr/>																	
1846	1856	1866	1876	1886	1896	1906											
<hr/>																	
CCCCCTGGTTC	GTCCCTGAGC	CTTTTCACA	GTGCATAAGC	AGTTTTTTTT	GTTTTGT TTT	TGTTTTGT TTT											
<hr/>																	
1916	1926	1936	1946	1956	1966	1976											
<hr/>																	
TGTTTTAAAA	TCAATCATGT	TACACTAATA	GAAACTTGGC	ACTCCTGTGC	CCTCTGCCTG	GACAAGCACA											
<hr/>																	
1986	1996	2006	2016	2026	2036	2046											
<hr/>																	
TAGCAAGCTG	AACTGTCC TA	AGGCAGGGGC	GAGCACGGAA	CAATGGGGCC	TTCAGCTGGA	GCTGTGGACT											
<hr/>																	
2056	2066	2076	2086														
<hr/>																	
TTTGTACATA	CACTAAAATT	CTGAAGTTAA	AGCTCAAAAAA	AA													

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FIG. 22

GA ATT CCA CAA CGG TTT CCC TCT AGA AAT TTT GTT TAA CTT GAA GGA GAT ATA CAT

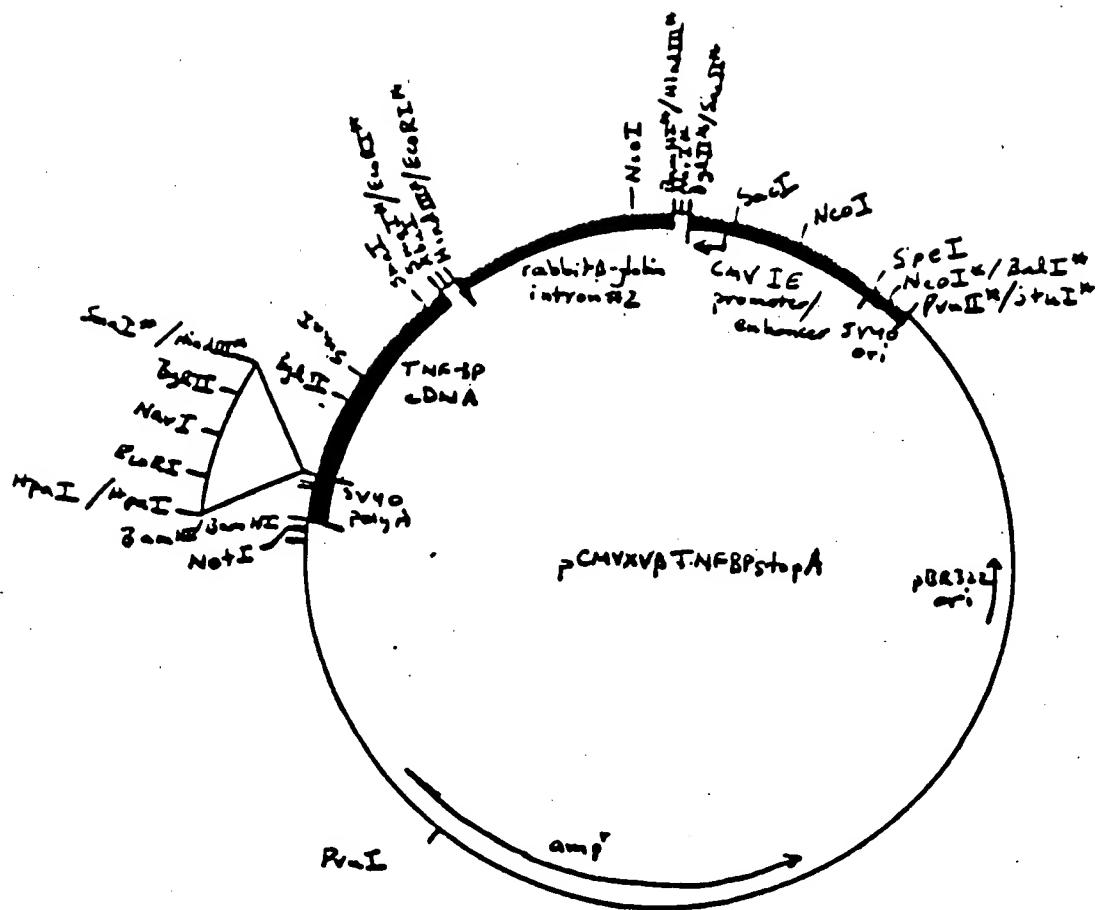
Start gene 10 protein sequence

ATG GCT AGC ATG ACT GGT GGA CAG CAA ATG GGT ACG GAT CCG ATC TTG GAG GAT GAT TAA
Met Ala Ser Met Thr Gly Gly Gln Gln Met Gly Thr Asp Pro Ile Leu Glu Asp Asp Stop

}

ATG GAC AGC GTT TGC CCC
Met ASP Ser Val Cys Pro
Start TNF inhibitor Sequence

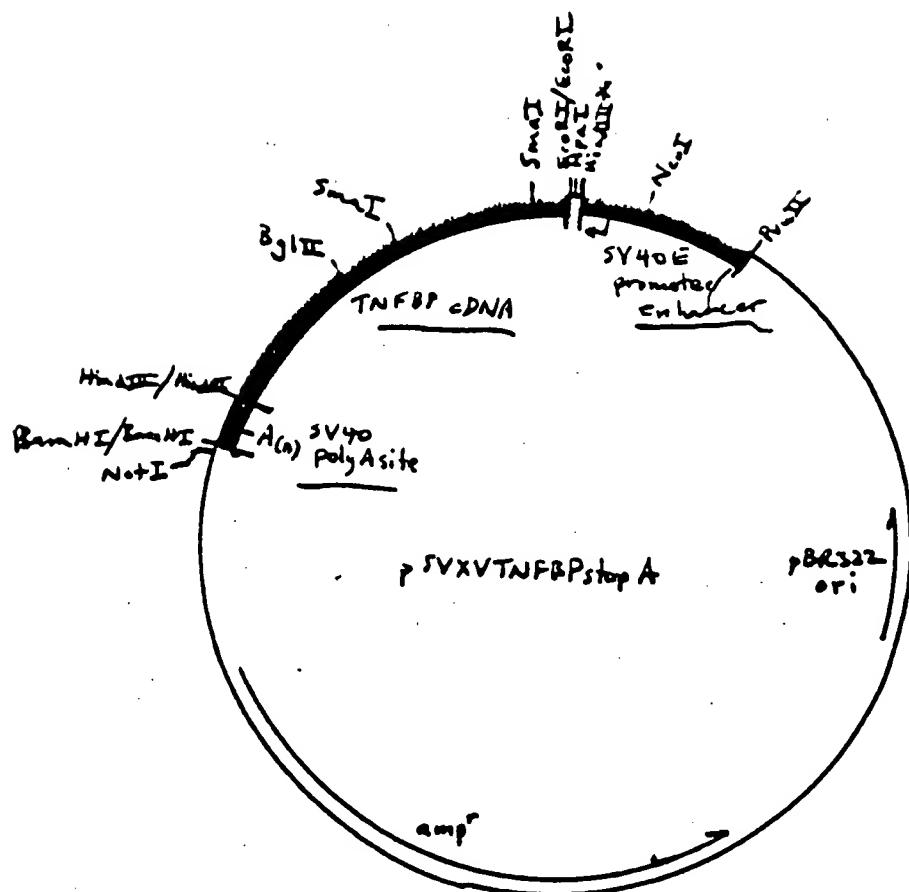
Fig. 23



* - indicates restriction site no longer exists.

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Fig. 24



* - restriction site no longer exists.

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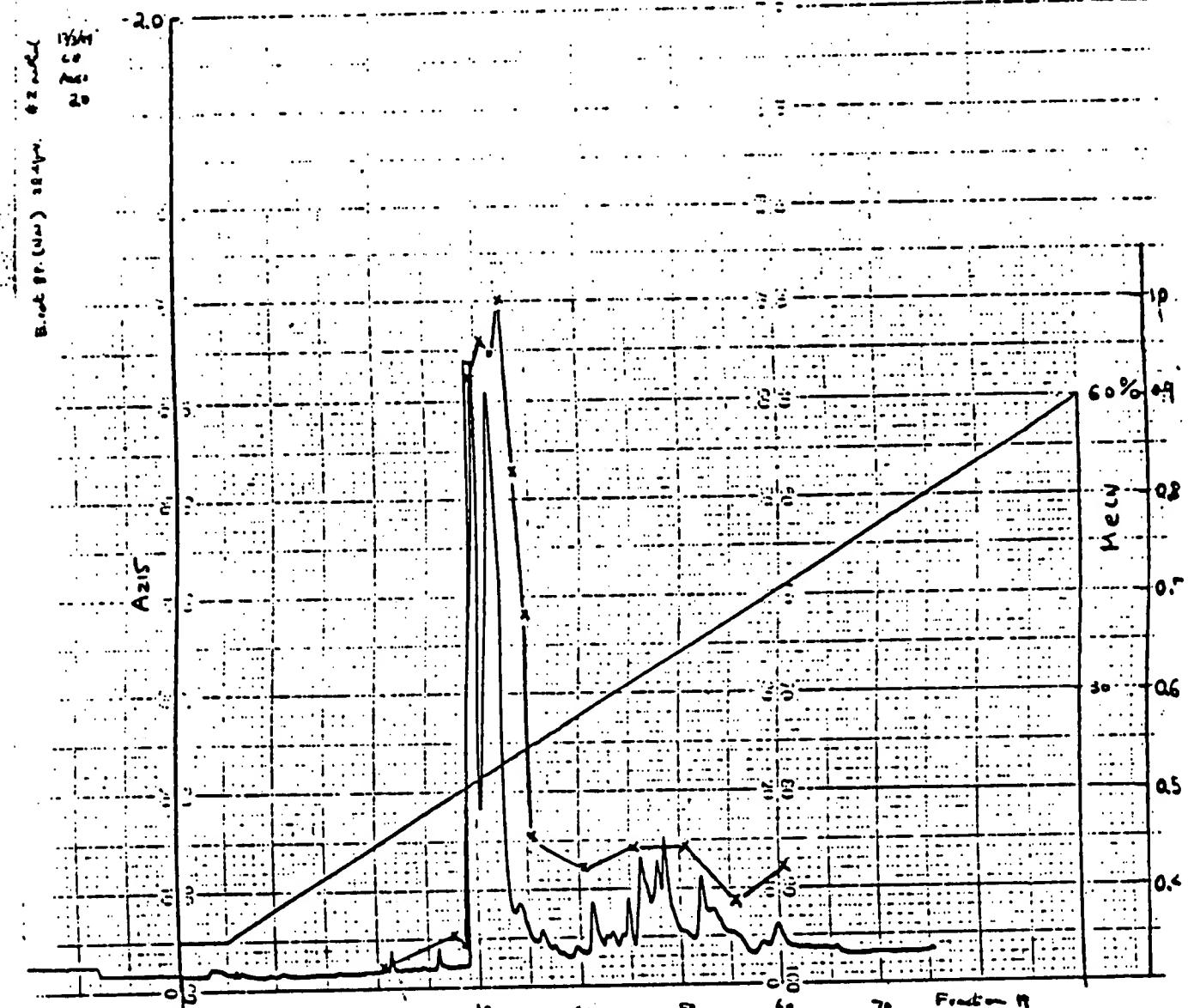


Figure 25

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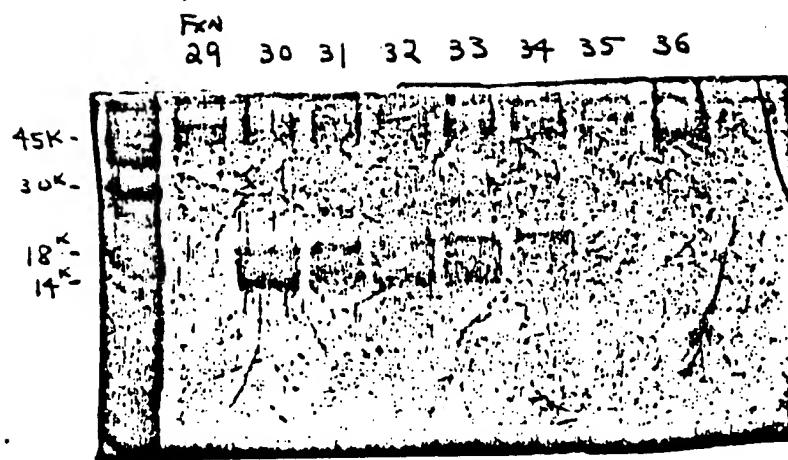


Figure 26

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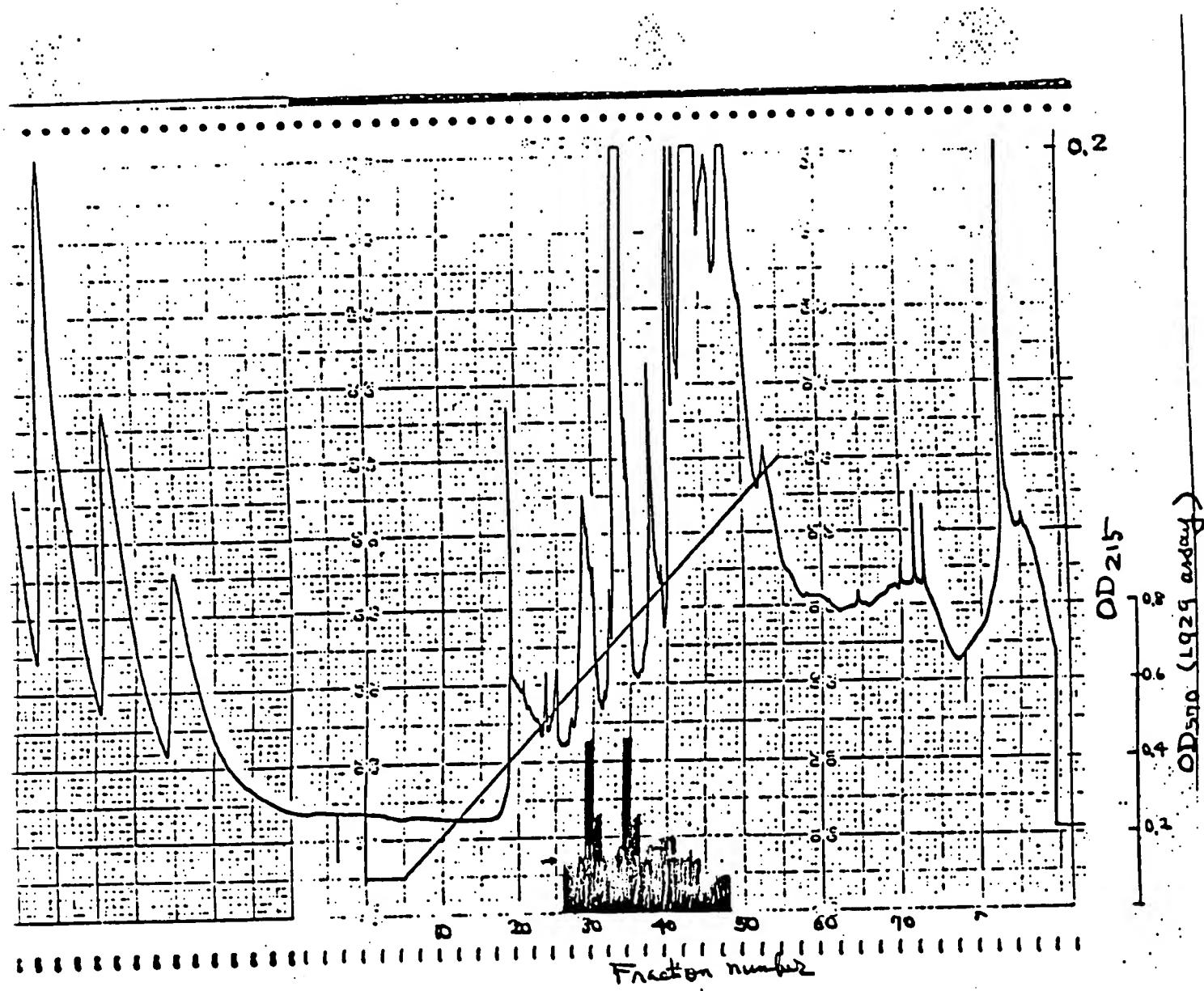
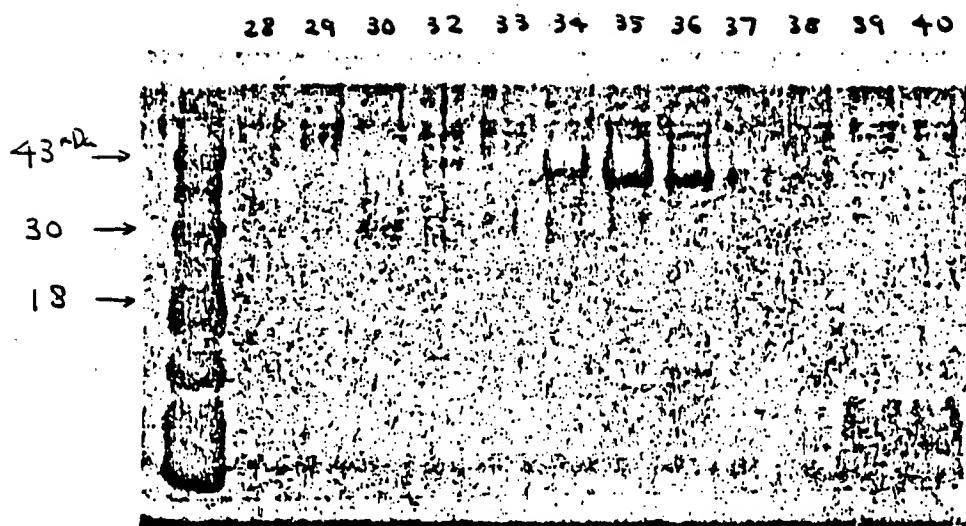


Fig. 27

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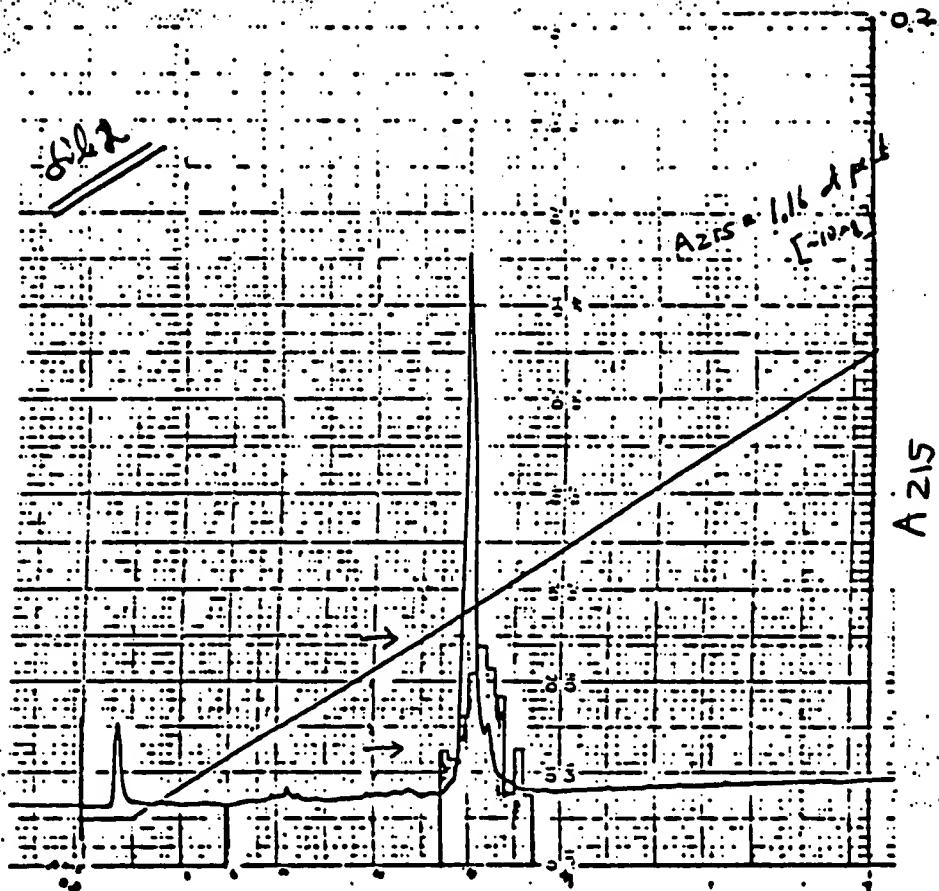
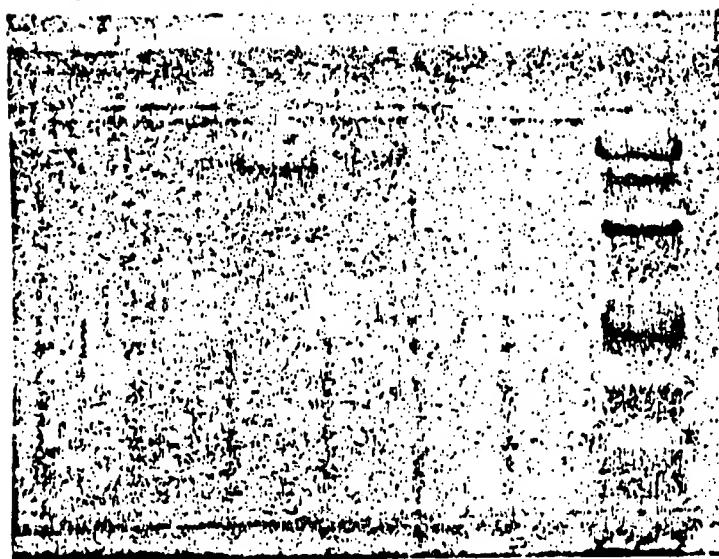


Fig. 29

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34 33 32 31 30 29



← 43 kDa
← 30 kDa
← 18 kDa

Fig 30

Fig. 31

U937-derived TNF-INH1 (30 kDa)

() - () - Val - () - Pro - Gln - GLY - Lys - Tyr - Ile - His - Pro - Gln -
() - Asn - () - Ile

U939-derived TNF-INH2 (40 kDa)

Leu - Pro - Ala - Gln - Val - Ala - Phe - Thr - Pro - Tyr - Ala - Pro - Glu - Pro - Gly -
Ser - Thr - Cys - Arg - Leu - Arg - Glu - Tyr - Tyr - Asp - Gln - Thr - Ala - Gln - Met -
Cys - Cys - Ser - Lys - Cys -

Urine-derived TNF-INH2 (40 kDa)

Ala - Gln - Val - Ala - Phe - Thr - Pro - Tyr - Ala - Pro - Glu - Pro - Gly - Ser - Thr -
Cys - () - Leu - () - Glu

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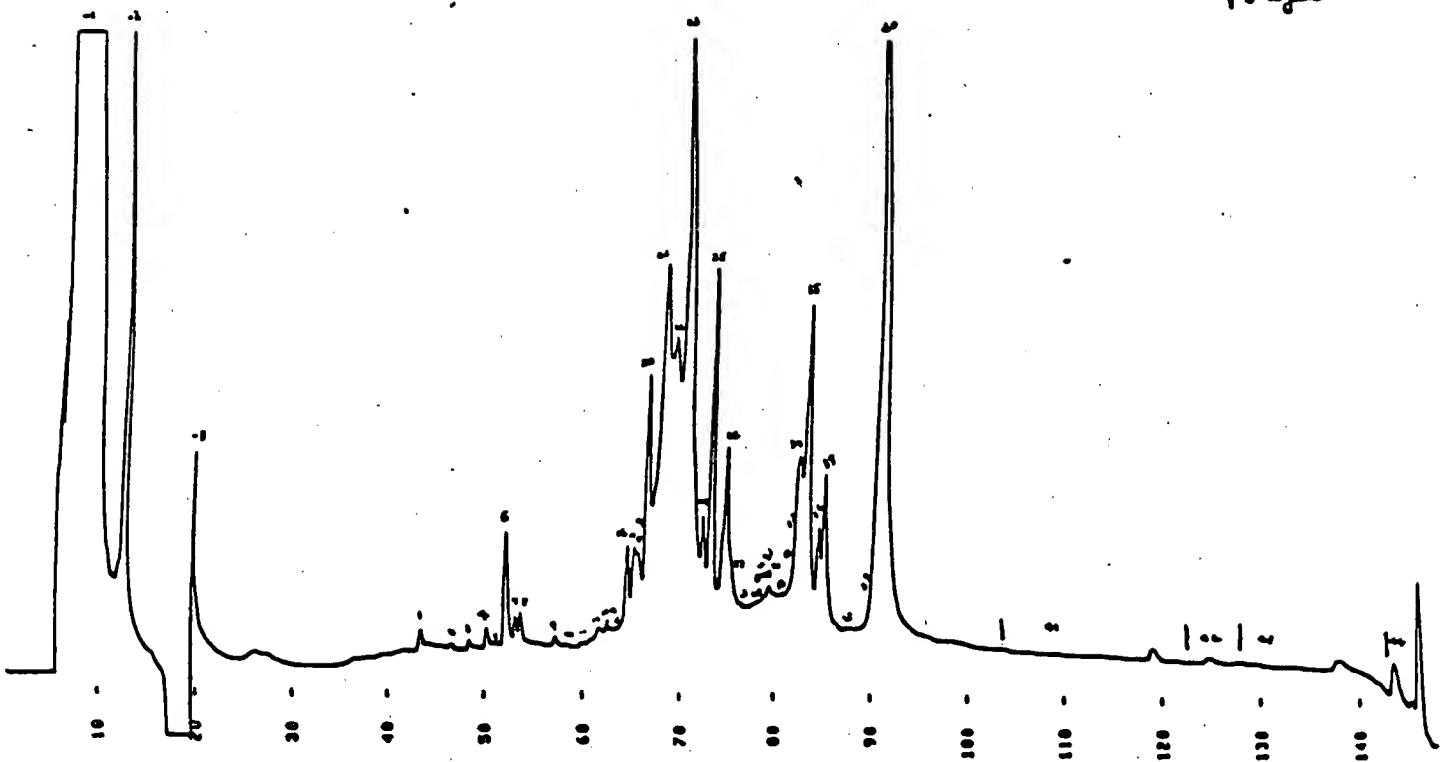


Figure 32

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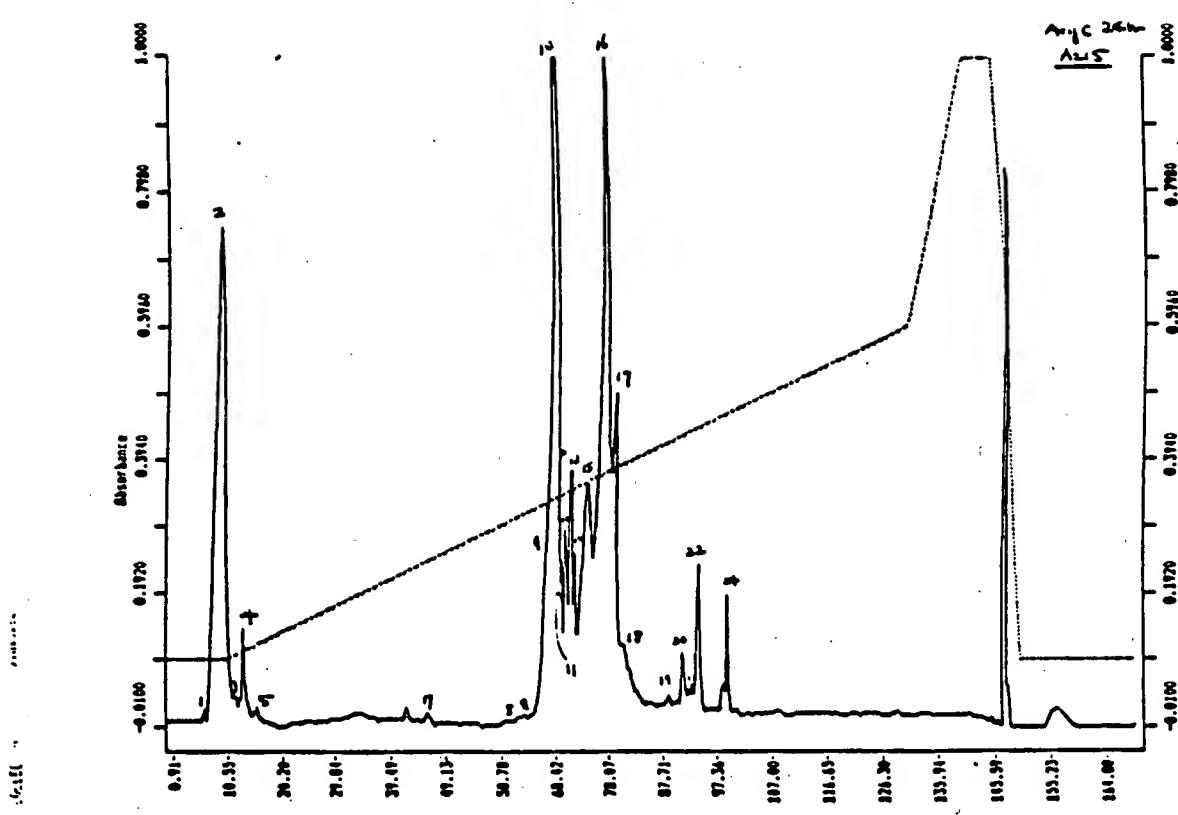


Figure 33

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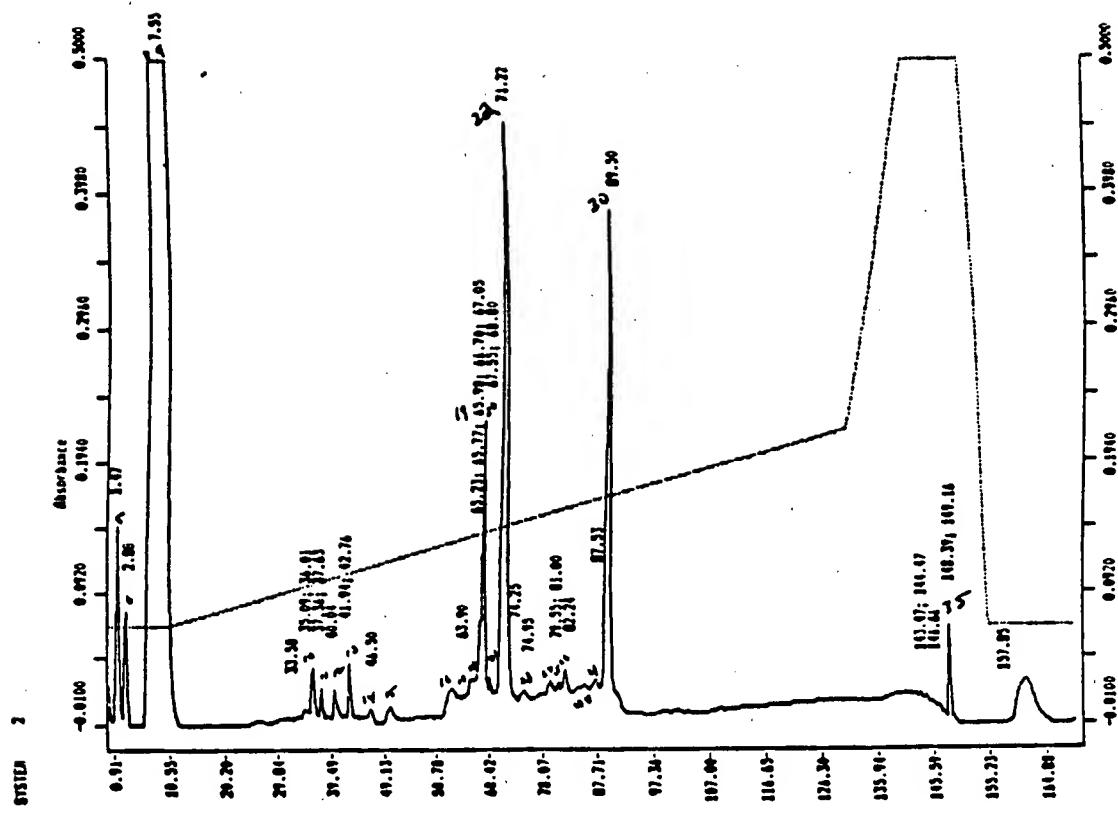


Figure 34

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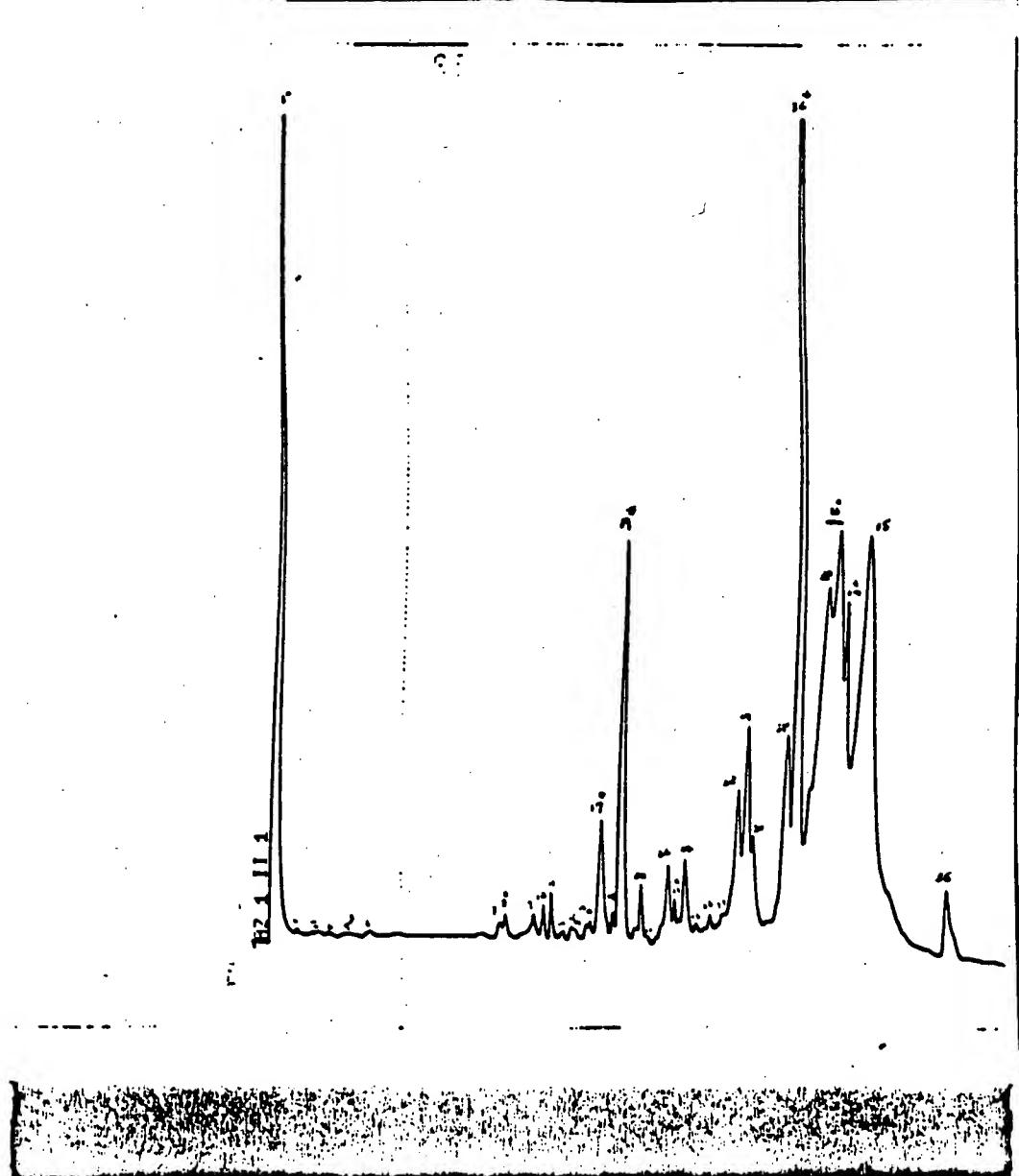


Figure 35

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1. R A Q V A F T P Y A P E R G S T C R L R E V Y D Q Q T A Q H C C S K C S P G Q H A K V F C T K T S O T V C O S C 2 0 S T Y T Q L - N - V P E C L S C G S R C S S

N T
V 25
R 12
V 34.35
R 16
V 37
R 4
V 6

R 16
R 16 T 30
R 16 T 30 V 9
R 4
R 16 T 30 V 4

D Q V E - - A C T R E Q H R I C T C R P G H Y C A L S K Q E C C R L C A P L R K C R P G F G V A R P G T E T S D V V C K P C A P G T F S - T T S S (T)D(X)P)(R/P)

V 20
R 4
R 14
V 23
R 16 T 13
R 10
R 10
R 10 C 19
R 10 C 32
R 10 C 17

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Figure 37

5' - CCG
Pro

5'	64	73	62	91	100
GAG CCC GCG AGC ACA TGC CGG CTC AGA GAA TAC TAT GAC CAG ACR GCW C4R ATG					
Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln MET					
109	118	127	136	145	154
TGC TGC AGC AAG TGC TCG CCG GGC CAA CAT GCA AAA GTC TTC TGT ACC AAG ACC					
Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr					
163	172	181	190	199	208
TCC GAC ACC GTG TGT SAC TCC TGT GAG GAC A3C HCH TAC ACC C4G CTC TGG AAC					
Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn					
217	226	235	244	253	262
TGG GTT CCC GAG TGC TTG AGC TGT GGC TCC CGC TGT AGC TCT GAC CAG GTG GAA					
Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu					
271	280	289	298	307	316
ACT CAA GCC TGC ACT CGG GAA CAG AAC CGC ATC TGC ACC TBC AGG CCC GGC TGG					
Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp					

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TAY TGC | - 3'
Tyr Cys

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Figure 38

Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser
Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln MET Cys Cys
Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr
Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu
Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser
Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys
Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys
Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala
Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro
Gly Thr Phe Ser Asn Thr Ser Ser Thr Asp Ile Cys Arg Pro His
Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Arg Asp Ala
Val Cys Thr Ser Thr Ser Pro Thr Arg Ser MET Ala Pro Gly Ala Val
His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr
Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro MET Gly
Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp

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DAATTCTGGCG CAGCGCG TGTAGAGAAG GCGCTGGGCT CGAGAGGCCGAGGGGAA GGGCAGGGGG

10 30 40 50 70

80	90	101	110	119	
CAACGGGACC CGGCCGAC CC ATG GCG CCC GTC GCC GTC TGG GCC GCG CTG GCC MET Ala Pro Val Ala Val Trp Ala Ala Leu Ala					
128	137	146	155	164	173
GTC GGA CTG GAG CTC TGG GCT GCG GCG CAC GCC TTG CCC GCC CAG GTG GCA TTT Val Gly Leu Glu Leu Trp Ala Ala His Ala Leu Pro Ala Gin Val Ala Phe					
182	191	200	209	218	227
ACA CCC TAC GCC CCG GAG CCC GGG ABC ACA TGC CGG CTC AGA GAA TAC TAT GAC Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp					
236	245	254	263	272	281
CAG ACA GCT CAG ATG TGC TGC AGC AAG TGC TCG CCG GGC CAA CAT GCA AAA GTC Gln Thr Ala Gln MET Cys Cys Ser Lys Cys Ser Pro Glu Gln His Ala Lys Val					
290	299	308	317	326	335
TTC TGT ACC AAC ACC TCG GAC ACC GTC TGT GAC TCC TGT GAG GAC AGC ACA TAC Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr					
344	353	362	371	380	389
ACC CAG CTC TGG ANC TGG GTT CCC GAG TGC TTG AGC TGT GGC TCC CGC TGT AGC Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Glu Ser Arg Cys Ser					
398	407	416	425	434	443
TCT GAC CAQ GTG GAA ACT CAA GCC TGC ACT CGG GAA CAG AAC CGC ATC TGC ACC Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr					
452	461	470	479	488	497
TGC AGG CCC GGC TGG TAC TGC GCG CTG AGC AAG CAG GAG GGG TGC CGG CTG TGC Cys Arg Pro Glu Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys					
506	515	524	533	542	551
GCB CGG CTG CGC AAC TGC CGC CCG GGC TTC GGC GTG GGC AGA CCA GGA ACT GAA Ala Pro Leu Arg Lys Cys Arg Pro Glu Phe Gly Val Ala Arg Pro Glu Thr Glu					
560	569	578	587	596	605
ACA TCA GAC GTG GTG TGC AAG CCC TGT GCC CCG GGG AGC TTC TCC AAC AGC ACT Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Glu Thr Phe Ser Asn Thr Thr					
614	623	632	641	650	659
TCA TCC ACU ATT TGC AAG CCC CAC CAG ATC TGT AAC GTG GTG GCG ATC CCT Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro					
668	677	686	695	704	713
GGG AAT GCA AGC AGG GAT GCA GTC TGC ACG TCC AGC TCC CCC ACC CGG AGT ATG Gly Asn Ala Ser Arg Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser MET					
722	731	740	749	758	767
GUC CCA GUG GCA GTA CAC TTA CCC CAG CCA GTG TCC ACA CCA TCC CAA CAC ACU Ala Pro Glu Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr					
776	785	794	803	812	821
CAG CCA ACT CCA GAA CCC AGC ACT GCT CCA AGC ACC TCC TTC CTG CTC CCA ATG Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro MET					
830	839	848	857	866	875
GGC CGC AGC CCC CCA GCT GAA GGG ABC ACT GCG GAC TTC GCT CTT CCA GTT GGA Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Glu					
884	893	902	911	920	929
CTG ATT GTG GGT GTG ACA GCC TTG GGT CTA CTA ATA ATA GGA GTG GTG AAC TGT Leu Ile Val Glu Val Thr Ala Leu Ile Leu Ile Ile Gly Val Val Asn Cys					
938	947	956	965	974	983
GTC ATC ATG ACC CAG GTG AAA AAG AAG CCC TTG TGC CTG CAG AGA GAA GCG AAG Val Ile MET Thr Gln Val Lys Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys					
992	1001	1010	1019	1028	1037
GTA CCT CAC TTG CCT GCC GAT AAG CGG BGT AGA CAG FGC CCC GAG CAG CAB Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Glu Pro Glu Gln Gln					

Figure
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1046	1059	1064	1073	1082		
CAC CTG CTG ATC ACA GCG CCG AGC TCC AGC AGC AGC TCC CTG GAG AGC TCG GCC His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala						
1100	1109	1118	1127	1136	1145	
AGT GCG TTG GAC AGA AGG BCG CCC ACT CGG AAC CAG CCA CAG GCA CCA GGC GTG Ser Ala Leu Asp Arg Arg Ala Pro Thr Arg ASN Glu Pro Glu Ala Pro Gly Val						
1154	1163	1172	1181	1190	1197	
GAG GCC AGT GGG GCC GGG GAG GCC CGG. GGC AGC ACC GGG AGC TCA GAT TCT TCC Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Asp Ser Ser						
1208	1217	1226	1235	1244	1253	
CCT GGT GGC CAT GGG ACC CAG BTC AAT BTC ACC TGC ATC GTG AAC BTC TGT AGC Pro Gly Gly His Gly Thr Glu Val ASN Val Thr Cys Ile Val ASN Val Cys Ser						
1262	1271	1280	1289	1298	1307	
AGC TCT GAC CAC AGC TCA CAG TCC TCC CAA GCC AGC TCC ACA ATG GGA GAC Ser Ser Asp His Ser Ser Glu Ser Ser Glu Ala Ser Ser Thr MET Gly Asp						
1316	1325	1334	1343	1352	1361	
ACA GAT TCC AGC CCC TCG GAG TCC CCG ANG GAC GAG CAG GTC CCC TTC TCC AAG Thr Asp Ser Bur Pro Bur Glu Bur Pro Lys Asp Glu Glu Val Pro Phe Ser Lys						
1370	1379	1388	1397	1406	1415	
GAG GAA TGT BCC TTT CGG TCA CAG CTG GAG AGC CCA GAG ACC CTG CTG GGG AGC Glu Glu Cys Ala Phe Arg Ser Glu Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser						
1424	1433	1442	1451	1460	1469	
ACC GAA GAG AAG CCC CTG CCC CTT GGA GTG CCT GAT GCT GUG ATG AAG CCC AGT Thr Glu Glu Lys Pro Leu Pro Glu Val Pro Asp Ala Gly MET Lys Pro Ser						
1478	1488	1498	1508	1518	1528	1538
TAA CCAGGCCGGT GTGGGCTBGB TCGTAGCCAA GGTGGGCTGA GCGCTGGCAG BATGACCCCTG						
1548	1558	1568	1578	1588	1598	1608
CGAAGGGGCC CTGGTCTTC CAGGCCCGCA CCACCTAGGAC TCTGGGGCTC TTTCTGGGCC AAGTTCCCT						
1618	1628	1638	1648	1658	1668	1678
AGTGGCCCTCC AAGGCCGCA CTCCTCTG ACCTGCAGGC CAAGAAGAGA UGCAGCGGGT TGTTGAAAAGC						
1688	1698	1708	1718	1728	1738	1748
CTCTGGCTGCC ATGGTGTATC CCTCTTGAA GGTGGCTGAGT GCATGGACGT TCCTGGCTCATG CTGGGGGCCAG						
1758	1768	1778	1788	1798	1808	1818
TCCCTUACTC TCTGTGACCT GCCCCGCCCA CCTGCACCTG CCAGCCTGGC TTCTGGAGCC CTTGGUTTT						
1828	1838	1848	1858	1868	1878	1888
TGTGTTGTTT GTTTGTTGTT TTGTTGTTT CTGGGGCTGG GCTCTGGCCC AGCTCTGGCT TCCAGAAAAC						
1898	1908	1918	1928	1938	1948	1958
CCACGCACTCC TTCTGCAAG AGGGGGCTTTC TGGAGAGGAG GGTGGCTGCC TGAGTCACCC ATGAAGACAG						
1968	1978	1988	1998	2008	2018	2028
GACAGTGGCT CAAGCTGAGG CTGAGAGCTGC UGGATGGTCC TGGGGCTCTG TGCAAGGGAGG AGGTGGCAGC						
2038	2048	2058	2068	2078	2088	2098
CCTGTAAGGA ACUUGGGTCTC TCAAGTTAAGC TCAGGGAGCT TGGAAAGCAT CACCTGAGGC CACTGTCGCC						
2108	2118	2128	2138	2148	2158	2168
ACCCGGATT AAACCTTTTA TCTCCCAAAT GGAAATATAA GAACTGTGCC TTTCTATCAC AAAAGGGAGAT						
2178	2188	2198	2208	2218		
TGTGABCAG AGGUCAATTA ATAATATGCG CCAAATAATT AAAAARACCG AATTC						

Figure
39 cont.

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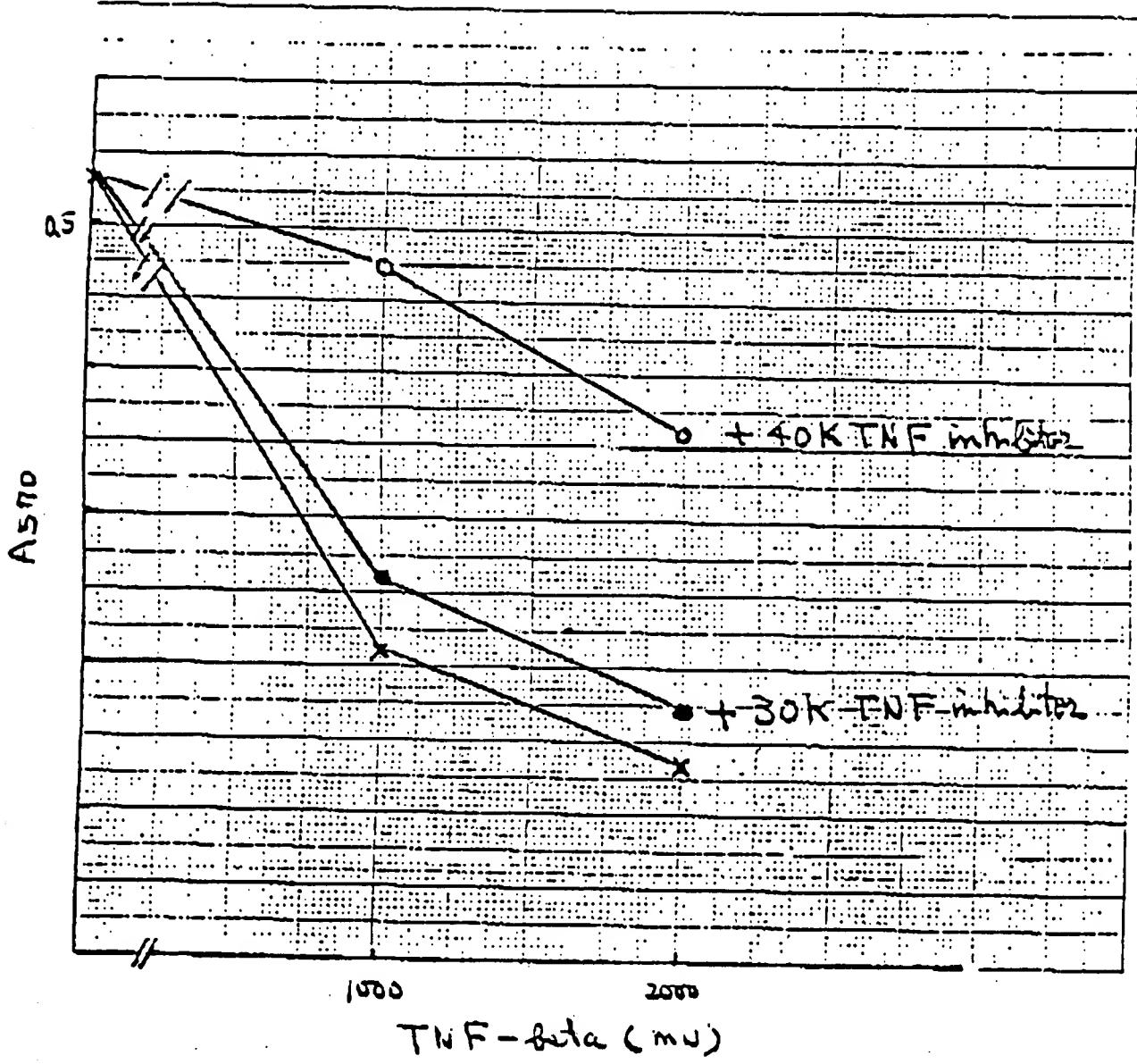
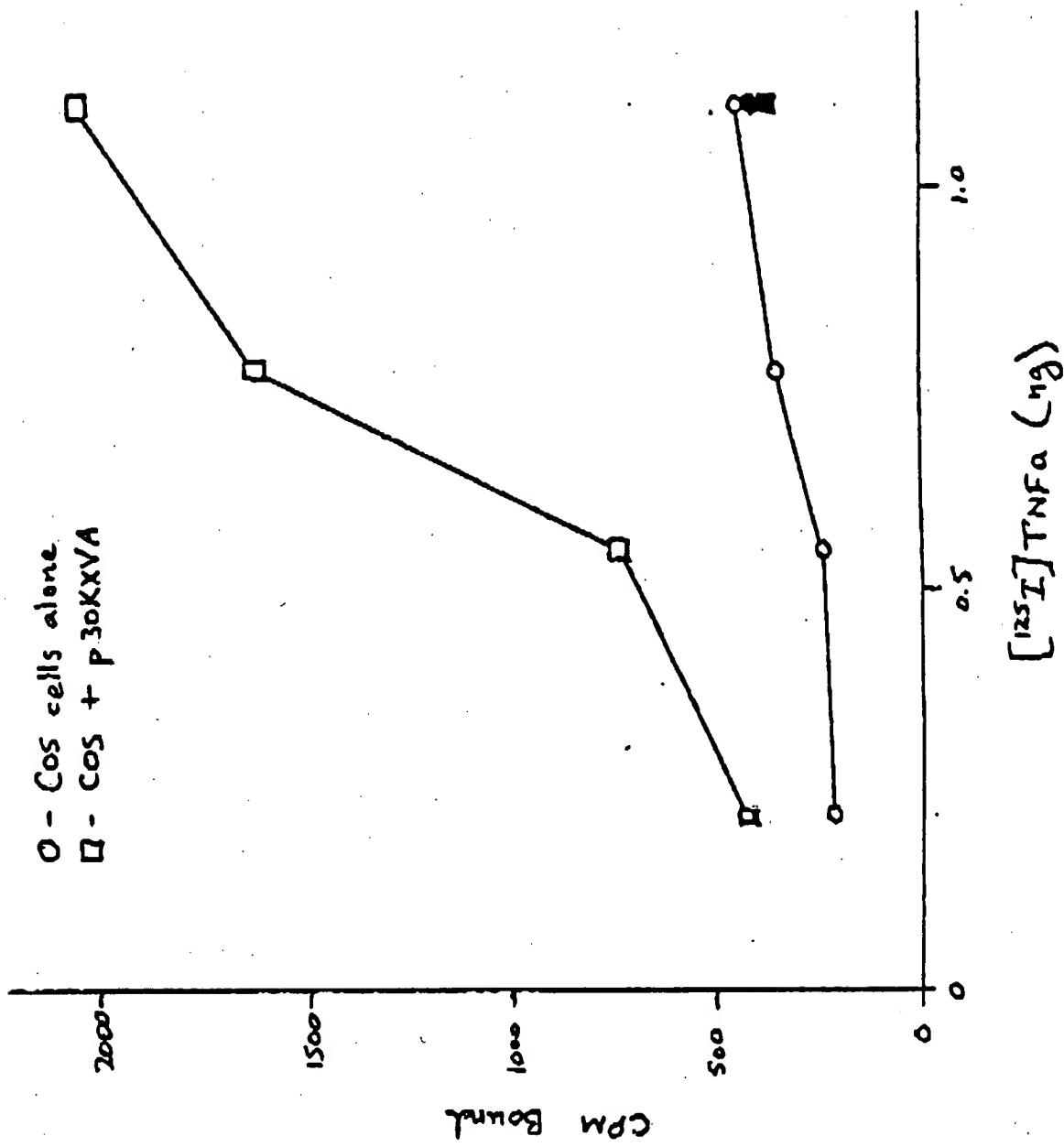


Figure 40

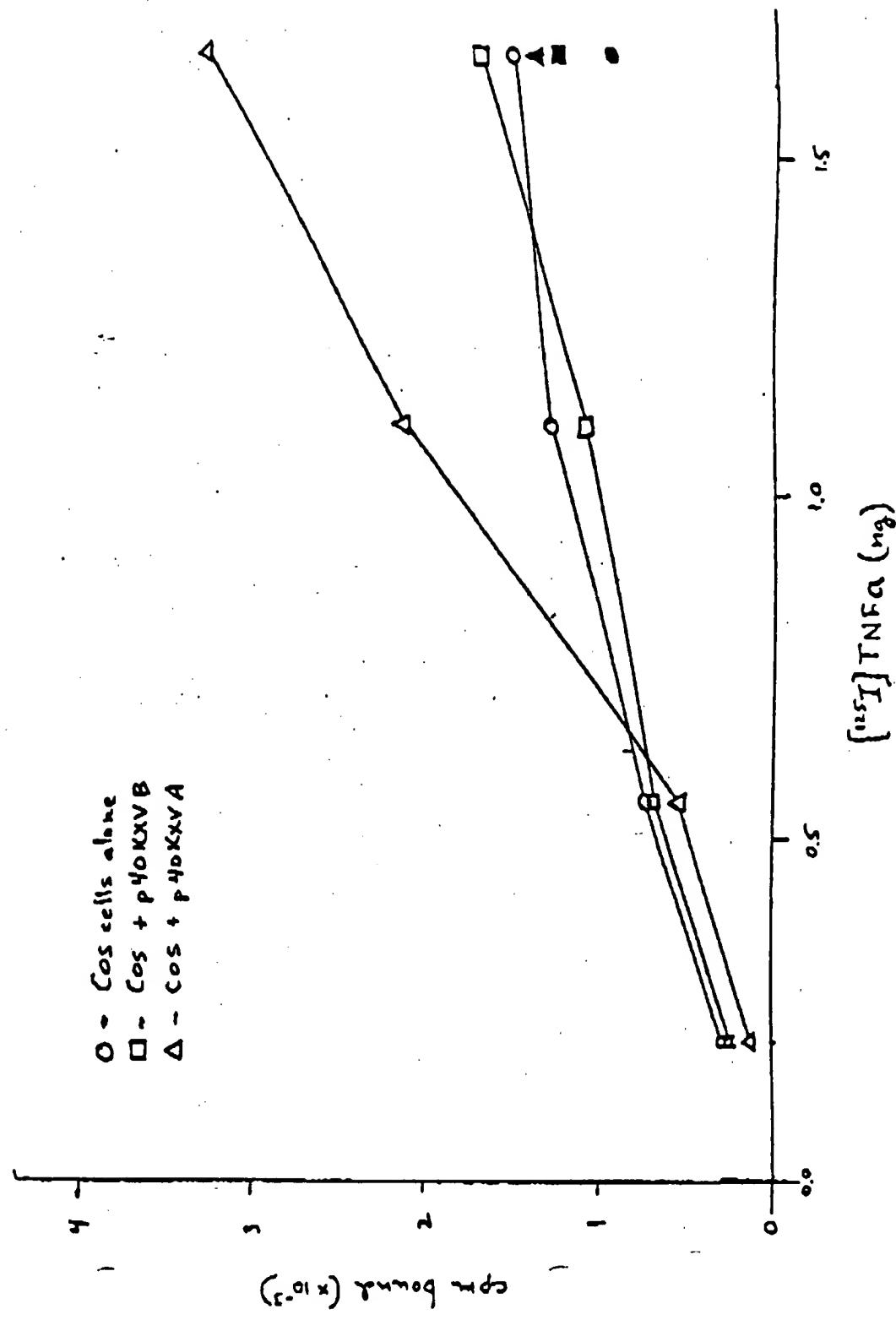
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Figure 41



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Figure 42



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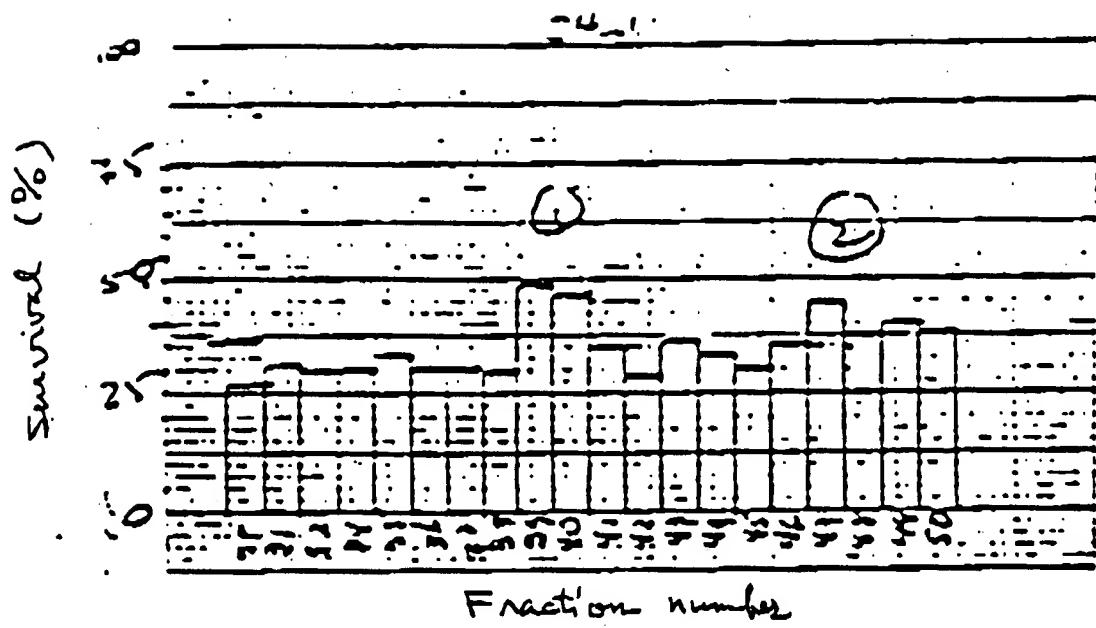
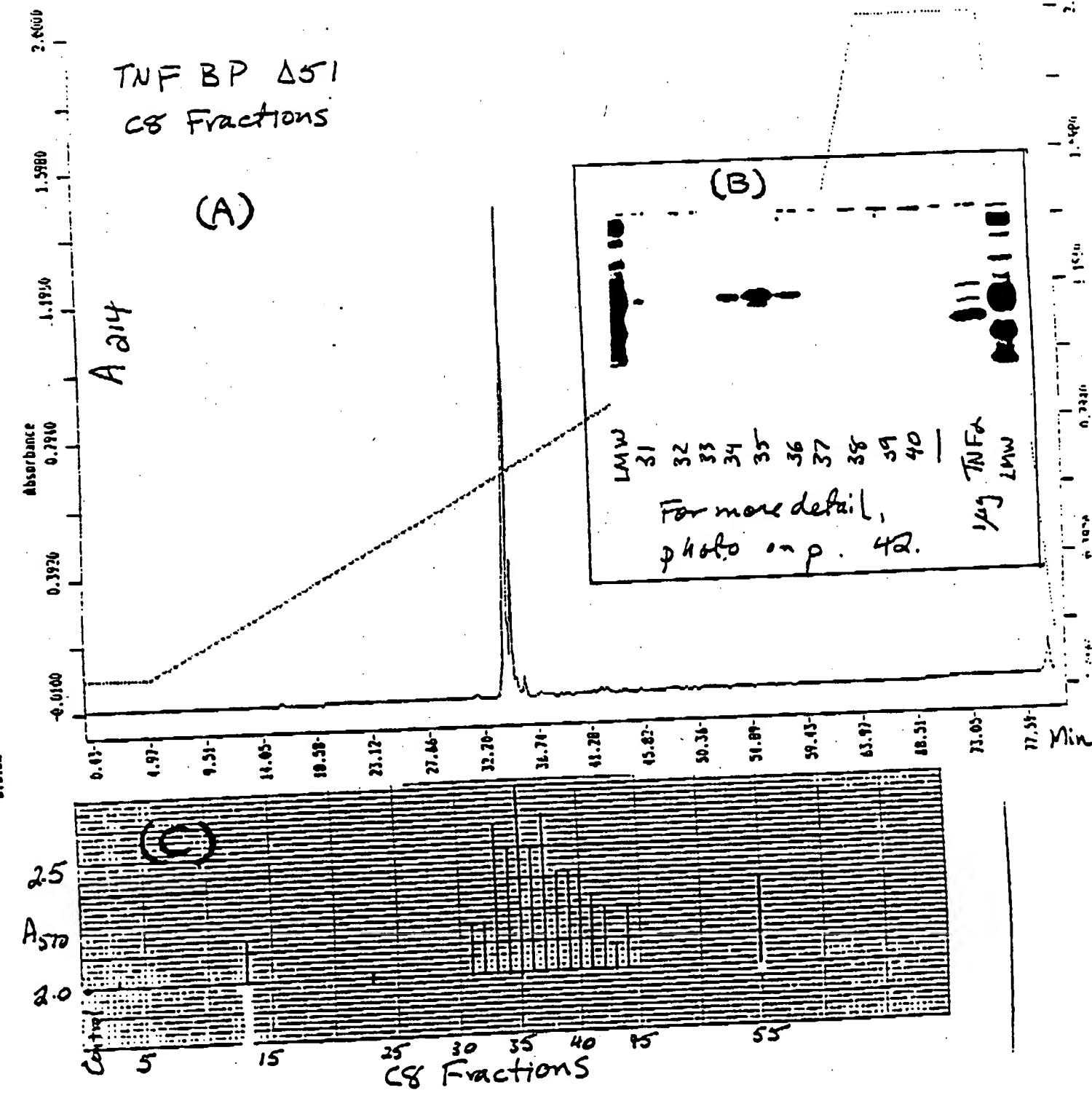


FIG 43

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FIG 44



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FIG. 45

